

BOSNIAN JOURNAL OF HEALTH SCIENCES AND TECHNOLOGIES (BJHST)

**Journal of the Discipline for Research and Development
Clinical Center University of Sarajevo**





130 GODINA USPJEŠNOG RADA KCUS

**BOSNIAN JOURNAL OF HEALTH
SCIENCES AND TECHNOLOGIES (BJHST)**

Vol. 2, No. 2, 2026

PUBLISHER

Discipline for Research and Development
Clinical Center University of Sarajevo
71 000 Sarajevo, Bolnička 25
Bosnia and Herzegovina

AIMS AND SCOPE

Bosnian Journal of Health Sciences and Technologies publishes original research articles, professional, review and educative articles, case reports, criticism, reports, professional news and other articles in the field of health sciences and technologies.

The journal is referral based, it follows a relevant database and is published three times a year: January, May and September.

EDITORIAL OFFICE

Address:

Bosnian Journal of Health Sciences and Technologies (BJHST),
Discipline for Research and Development
Clinical Center University of Sarajevo
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ISSN 3029-4347 (Print)

ISSN 3029-4355 (Online)

<https://www.kcus.ba/casopis-bjhst/>

PRINT

Print Shop d.o.o.
East Sarajevo

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This project is supported by the Federal
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Prevalence of Factor II Prothrombin (G20210A) and Factor V Leiden (G1691A) Mutations in Pregnant Women with Spontaneous Miscarriage

Učestalost mutacija faktora II protrombina (G20210A) i faktora V Leiden (G1691A) kod trudnica sa spontananim pobačajem

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ABSTRACT

Introduction: Spontaneous miscarriage is the most common complication of early pregnancy, affecting 15-25% of all clinically confirmed pregnancies. Hereditary thrombophilia, particularly mutations in factor II prothrombin (FII G20210A) and factor V Leiden (FVL G1691A), has been implicated as a potential risk factor for recurrent pregnancy loss due to hypercoagulability and placental thrombosis.

Aim: to evaluate the frequency of FII G20210A and FVL G1691A mutations in pregnant women with indicated spontaneous miscarriages and to assess their association with adverse pregnancy outcomes.

Materials and Methods: This observational study included 1,433 pregnant women with a history of indicated spontaneous miscarriage over a five-year period (2018–2022). DNA was extracted from peripheral blood samples, and genotyping for FII G20210A and FVL G1691A mutations was performed using real-time PCR. Descriptive statistics and Chi-

square tests were applied, with statistical significance set at $p < 0.05$.

Results: The frequency of heterozygous FII mutation was 3.9% (57/1,433), while homozygous FII mutation was observed in only 0.07% (1/1,433). Heterozygous FVL mutation was present in 10.5% (150/1,433), and homozygous FVL mutation in 0.14% (2/1,433). Wild-type genotype for both factors was found in 79.8% (1,143/1,433). A statistically significant association was observed between the presence of FVL mutation and the incidence of deep vein thrombosis (DVT) and pulmonary embolism (PE) in 2018, 2020, 2021 and 2022 ($p < 0.05$).

Conclusion: Heterozygous FVL mutation is present in approximately one in ten pregnant women with spontaneous miscarriage in our population, while FII mutation is less common. The significant association between FVL mutation and thromboembolic complications supports the clinical utility of genetic testing in this high-risk population.

Keywords: spontaneous miscarriage, factor II prothrombin, factor V Leiden, thrombophilia, pregnancy

SAŽETAK

Uvod: Spontani pobačaj je najčešća komplikacija rane trudnoće i javlja se u 15–25% svih klinički potvrđenih trudnoća. Nasljedna trombofilija, posebno mutacije faktora II protrombina (FII G20210A) i faktora V Leiden (FVL G1691A), prepoznata je kao potencijalni faktor rizika za ponavljajuće gubitke trudnoće zbog hiperkoagulabilnosti i placentalne tromboze.

Cilj: ispitati učestalost mutacija FII G20210A i FVL G1691A kod trudnica sa indiciranim spontanim pobačajem i procijeniti njihovu povezanost s nepovoljnim ishodima trudnoće.

Materijali i metode: Ovo opservacijsko istraživanje uključilo je 1.433 trudnice sa indiciranim spontanim pobačajem tokom petogodišnjeg perioda (2018–2022). DNK je izolirana iz uzoraka periferne krvi, a genotipizacija za mutacije FII G20210A i FVL G1691A urađena je korištenjem PCR metode u realnom vremenu. Primijenjene su deskriptivne statističke metode i Hi-kvadrat test, uz nivo statističke značajnosti $p < 0,05$.

Rezultati: Učestalost heterozigotne FII mutacije iznosila je 3,9% (57/1.433), dok je homozigotna FII mutacija uočena u samo 0,07% (1/1.433). Heterozigotna FVL mutacija bila je prisutna u 10,5% (150/1.433), a homozigotna FVL mutacija u 0,14% (2/1.433). Wild-type genotip za oba faktora nađen je u 79,8% (1.143/1.433). Utvrđena je statistički značajna povezanost između prisustva FVL mutacije i incidencije duboke venske tromboze (DVT) i plućne embolije (PE) u 2018, 2020, 2021 i 2022. godini ($p < 0,05$).

Zaključak: Heterozigotna FVL mutacija prisutna je kod otprilike jedne od deset trudnica sa spontanim pobačajem u našoj populaciji, dok je FII mutacija rjeđa. Značajna povezanost između FVL mutacije i tromboembolijskih komplikacija podržava kliničku

korisnost genetskog testiranja u ovoj rizičnoj populaciji.

Ključne riječi: spontani pobačaj, faktor II protrombin, faktor V Leiden, trombofilija, trudnoća

INTRODUCTION

Spontaneous miscarriage is defined as the spontaneous loss of a pregnancy before the fetus reaches viability, typically before 20–24 weeks of gestation or when the fetus weighs less than 500–1000 grams. It occurs in approximately 15–25% of all clinically recognized pregnancies, making it the most common complication of early pregnancy (1,2). Recurrent pregnancy loss (RPL), defined as two or more consecutive miscarriages, affects approximately 1-5% of couples and represents a significant clinical and emotional challenge (3).

The etiology of spontaneous miscarriage is multifactorial and includes chromosomal abnormalities (accounting for approximately 50% of early miscarriages), anatomical anomalies of the uterus, endocrine disorders, immunological factors, infections, and thrombophilias (4,5). Despite extensive diagnostic workup, a definitive cause remains unidentified in approximately 50% of cases (6).

Hereditary thrombophilia, particularly the factor V Leiden (FVL) G1691A mutation and the factor II prothrombin (FII) G20210A mutation, has emerged as an important risk factor for pregnancy loss. These mutations predispose to a hypercoagulable state by impairing the natural anticoagulant pathways, leading to increased risk of thrombosis in the placental vasculature and subsequent pregnancy complications (7,8).

Factor V Leiden mutation, the most common inherited thrombophilia in Caucasian populations, results from a single nucleotide substitution (G1691A) that renders activated factor V resistant to degradation by activated protein C (APC resistance). Heterozygous carriers have a 3–7 fold increased risk of venous thromboembolism (VTE), while homozygotes have an 80-90 fold increased risk (9).

The prevalence of FVL mutation varies geographically: approximately 4-7% in European populations, 2-3% in Middle Eastern populations, and is rare in Asian and African populations (10).

The prothrombin G20210A mutation is a missense mutation in the 3'-untranslated region of the factor II gene, resulting in elevated plasma prothrombin levels and increased thrombin generation. This mutation is present in approximately 2-3% of the European population and is associated with a 2–3 fold increased risk of VTE (11).

Both mutations have been implicated in adverse pregnancy outcomes, including recurrent miscarriage, intrauterine growth restriction (IUGR), preeclampsia, and placental abruption. The proposed mechanism involves thrombosis of the placental intervillous spaces, leading to placental insufficiency and fetal loss (12,13).

AIM

The aim of this study was to evaluate the frequency of FII G20210A and FVL G1691A mutations in pregnant women with indicated spontaneous miscarriages and to assess their association with thromboembolic complications (DVT and PE).

MATERIALS AND METHODS

This observational analytical study was conducted at the Department of Clinical Pathology, Cytology and Human Genetics of the Clinical Center University of Sarajevo over a five-year period, specifically from 2018 to 2022.

Study population

The study included a total of 1,433 pregnant women with a history of indicated spontaneous miscarriage. All participants were referred for genetic testing for hereditary thrombophilia based on clinical criteria including: history of venous thrombosis, pulmonary embolism, recurrent

miscarriages (≥ 2), unexplained thrombosis at young age, or failed IVF procedures. Women with incomplete medical documentation or known acquired thrombophilia (antiphospholipid syndrome) were excluded.

Sample collection and DNA extraction

Peripheral blood samples were collected in EDTA anticoagulant tubes under standard aseptic conditions. DNA extraction was performed using the DNA Sample Preparation Kit (Roche Diagnostics) according to the manufacturer's standardized protocol.

Genotyping

Genotyping for FII G20210A and FVL G1691A mutations was performed using real-time PCR on the LightCycler® 480 Instrument (Cobas Z 480) using Cobas® Factor II and Factor V Test reagents for SNP detection. Results were analyzed using LightCycler® 480 software.

Statistical analysis

Descriptive statistics were applied, including calculation of frequencies and percentages. The Chi-square test was used to assess associations between genetic mutations and the incidence of DVT and PE. Statistical significance was defined as $p < 0.05$.

Ethical considerations

The study was conducted in accordance with ethical standards for biomedical research. All participants provided informed consent for genetic testing.

RESULTS

The study included 1,433 pregnant women with indicated spontaneous miscarriage over the five-year period (2018-2022). Table 1 shows the distribution of participants by year and the frequency of FII and FVL mutations.

Table 1 Frequency of FII and FVL mutations in pregnant women (2018-2022).

Godina	Trudnice (N)	FII hetero n (%)	FII homo n (%)	FVL hetero n (%)	FVL homo n (%)	WT oba n (%)
2018	209	18 (8.61%)	0 (0%)	24 (11.48%)	0 (0%)	167 (79.9%)
2019	163	4 (2.45%)	0 (0%)	14 (8.59%)	1 (0.61%)	144 (88.3%)
2020	233	11 (4.72%)	0 (0%)	22 (9.44%)	0 (0%)	200 (85.8%)
2021	360	13 (3.61%)	0 (0%)	39 (10.83%)	1 (0.28%)	307 (85.3%)
2022	468	11 (2.35%)	1 (0.21%)	51 (10.90%)	0 (0%)	405 (86.5%)
Ukupno	1,433	57 (3.98%)	1 (0.07%)	150 (10.47%)	2 (0.14%)	1,223 (85.3%)

FII hetero - heterozygote for factor II prothrombin mutation; FII homo - homozygote for factor II prothrombin mutation; FVL hetero - heterozygote for factor V Leiden mutation; FVL homo - homozygote for factor V Leiden mutation; WT - wild type (no mutation).

The overall frequency of heterozygous FII mutation was 3.98% (57/1,433), while homozygous FII mutation was extremely rare (0.07%, 1/1,433). Heterozygous FVL mutation was found in 10.47% (150/1,433) of patients, and homozygous FVL mutation in 0.14% (2/1,433). The majority of patients (85.3%) had wild-type genotype for both factors.

Table 2 Comparison of mutation frequencies between the study groups.

Parametar	Ispitivana grupa (N=1,433)	Literatura (evropska populacija)	p-value
FII hetero	3.98%	2–3%	>0.05
FVL hetero	10.47%	4–7%	<0.05

The frequency of FVL heterozygosity in our study population (10.47%) was significantly higher compared to published prevalence in the general

European population (4-7%), suggesting an association between FVL mutation and spontaneous miscarriage.

Table 3 Association between FVL mutation and thromboembolic complications (DVT/PE).

Godina	Ukupno trudnica	FVL mutacija (hetero+homo)	DVT/PE incidenca	Chi-square	p-value
2018	209	24 (11.5%)	18 DVT, 0 PE	36.00	<0.001
2019	163	15 (9.2%)	4 DVT, 1 PE	0.27	0.606
2020	233	22 (9.4%)	11 DVT, 0 PE	6.44	0.011
2021	360	40 (11.1%)	13 DVT, 1 PE	15.58	<0.001
2022	468	51 (10.9%)	11 DVT, 0 PE	283.62	<0.001

A statistically significant association between FVL mutation and the incidence of DVT/PE was observed in four out of five years (2018, 2020, 2021, 2022; $p < 0.05$), while no significant association was found in 2019 ($p = 0.606$).

DISCUSSION

This five-year study evaluated the frequency of FII G20210A and FVL G1691A mutations in 1,433 pregnant women with indicated spontaneous

miscarriage. Our findings demonstrate that heterozygous FVL mutation is present in 10.47% of this population, which is significantly higher than the reported prevalence of 4–7% in the general European population (10,14). This observation supports the established association between FVL mutation and recurrent pregnancy loss.

The frequency of FVL heterozygosity in our study (10.47%) is consistent with previous meta-analyses. A systematic review and meta-analysis including 89 studies from 2021 demonstrated that women with FVL mutation have a significantly increased risk of RPL (odds ratio = 2.44) (15). Similarly, a meta-analysis of 19 case-control studies from Middle Eastern countries found a prevalence of FVL mutation of 12.6% in patients with RPL compared to 4.9% in controls (odds ratio = 2.37) (16). These findings align closely with our results.

The frequency of FII heterozygosity in our population was 3.98%, which is slightly higher than the reported 2-3% in European populations (11,17). Meta-analyses have consistently shown an association between FII mutation and RPL, with odds ratios ranging from 1.81 to 2.08 (18,19). The slightly elevated frequency in our study may reflect the selected high-risk nature of our cohort (all patients had indicated spontaneous miscarriage) or potential population-specific genetic variations in Bosnia and Herzegovina.

Homozygous mutations for both FII and FVL were extremely rare in our study (0.07% and 0.14%, respectively), which is consistent with their low prevalence in the general population. Homozygous FVL mutation is associated with an 80-90 fold increased risk of thrombosis [9], and its rarity in our cohort is expected.

Regarding the association with thromboembolic complications, we observed a statistically significant association between FVL mutation and the incidence of DVT/PE in four of the five study years (2018, 2020, 2021, 2022; $p < 0.05$). The lack of significant association in 2019 may be due to the smaller sample size that year (163 women) or other confounding factors. These findings are consistent

with the well-established role of FVL mutation in venous thromboembolism, particularly during pregnancy when the physiological hypercoagulable state exacerbates the thrombotic risk (20,21).

The pathophysiological mechanism linking FVL mutation to pregnancy loss involves thrombosis of the placental intervillous spaces. FVL mutation leads to APC resistance, resulting in uncontrolled thrombin generation and fibrin deposition in the placental microcirculation, which compromises fetal blood supply and leads to miscarriage (22,23). This mechanism is supported by histopathological findings of placental thrombosis in women with FVL mutation and recurrent miscarriage.

The clinical implications of our findings are significant. Given the high frequency of FVL mutation in our cohort (10.47%), genetic screening for thrombophilia mutations may be warranted in women with recurrent miscarriage, particularly in those with additional risk factors for thrombosis. Early identification of mutation carriers allows for appropriate antenatal surveillance and consideration of prophylactic anticoagulation with low-molecular-weight heparin, which has been shown to improve pregnancy outcomes in selected patients (24,25).

Limitations of the study include its cross-sectional design, which precludes assessment of causality, and the lack of a healthy control group of pregnant women without miscarriage. Additionally, the study was conducted at a single center, which may limit generalizability to other populations. Future prospective studies should include longitudinal follow-up and assessment of anticoagulation therapy outcomes.

CONCLUSION

This study confirms that hereditary thrombophilia mutations, particularly factor V Leiden G1691A, are present at elevated frequencies in pregnant women with indicated spontaneous miscarriage in Bosnia and Herzegovina. The frequency of heterozygous FVL mutation (10.47%) is significantly higher than in the general European population, supporting its role as a risk factor for pregnancy loss.

Key findings:

- **FVL heterozygosity** was the most common mutation, affecting approximately one in ten women (10.47%).
- **FII heterozygosity** was less common (3.98%), but still elevated compared to population prevalence.
- **Homozygous mutations** were extremely rare (0.07–0.14%).
- A **statistically significant association** was found between FVL mutation and DVT/PE complications in most study years.

The combined assessment of FII and FVL mutations provides valuable diagnostic and prognostic information in women with recurrent miscarriage. Genetic testing for these mutations should be considered as part of the standard diagnostic workup for recurrent pregnancy loss, as early identification may guide prophylactic anticoagulation and improve pregnancy outcomes.

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- Authors' Contributions:** AM, EH, ZH, IB, MH, BB, SDž and AO contributed significantly to the conception and design of the article, as well as the acquisition, analysis, and interpretation of data for the work. Each author had a role in drafting of the article and the revision process. Each author gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Financial Support and Sponsorship:** nil.
- Conflict of Interest:** there are no conflicts of interest.

Demonstration of Protein Kinase Zap-70 Expression in Cells of Patients With Chronic Lymphocytic Leukemia Using Flow Cytometry

Dokazivanje ekspresije protein kinaze zap-70 u stanicama pacijenata sa hroničnom limfatičnom leukemijom metodom protočne citometrije

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ABSTRACT

Introduction: Chronic Lymphocytic Leukemia (CLL) is a malignant disease of white blood cells, lymphocytes, characterized by a slow but progressive increase in the number of these cells in peripheral blood and bone marrow. Using flow cytometry in routine diagnostics, it was found that the population of monoclonal CD5 + B cells (CDs) can also be identified in adult healthy adults over the age of 40. Many of these clones occurring in a healthy population have genomic abnormalities associated with CLL, including 13q14 deletion and trisomy of chromosome 12, similar to those occurring in sporadic CLL cases. Diagnostic criteria for CLL include absolute mature lymphocytosis in peripheral blood which persists for at least three months and is clinically unexplained. The key immunophenomenon of the cells present is manifested by coexpression of B-lymphocytes on CD5, CD23 and CD19. In treating CLL prognostic factors play a significant role in determining individual therapy. The major prognostic markers CLL are the clinical phase of disease, cytogenetic abnormality, the IgHV gene mutation status of the Ig heavy chain variable

region genes (IgHV), zeta-assimilated 70 kDa protein (ZAP-70, Zeta-chain-associated protein kinase 70) and CD38 marker.

Aim: to introduce and standardize the ZAP-70 expression method in CLL patients using flow cytometry.

Materials and methods: The study was conducted on 35 patients whose sample was referred to the flow cytometry analysis for diagnosis. The referral diagnosis was chronic lymphatic leukemia.

Results: Using flow cytometry, it was found that ZAP-70 protein expression was well correlated with the presence of IgV mutation, although discordant cases were described and markers were free treatment and survival. Since flow cytometry was routinely used in CLL diagnosis, expression determination with ZAP-70 flow cytometry would be a widely used prognostic marker. The success of the method was determined by determining the correlation between ZAP-70 expression and the presence of ZAP-70 in T lymphocytes and NK cells

and correlation with gene mutations of patients with CLL.

Conclusion: Further work on standardization and immunophenotypic determination of ZAP-70 will be required. The ease of flow cytometry, which can be used for any new patient, along with the routine diagnostic test panel, can provide a powerful tool for prospective studies.

Keywords: chronic lymphocytic leukemia, flow cytometry, protein kinase Zap-70

SAŽETAK

Uvod: Hronična limfatična leukemija (CLL, engl. Chronic Lymphocytic Leukaemia) je maligna bolest bijelih krvnih stanica, limfocita, koju karakterizira spor, ali progresivan porast broja tih stanica u perifernoj krvi i koštanoj srži. Korištenjem protočne citometrije u rutinskoj dijagnostici, utvrđeno je da se populacija monoklonalnih CD5+ B stanica (CD, engl. clusters of differentiation) može identificirati i kod odraslih zdravih osoba starijih od 40 godina. Mnogi od ovih klonova koji se javljaju u zdravoj populaciji imaju genske abnormalnosti povezane sa CLL, uključujući 13q14 deleciju i trisomiju hromosoma 12, slično kao što se javlja u sporadičnim slučajevima CLL. Dijagnostički kriteriji za CLL uključuju absolutnu zrelu limfocitozu u perifernoj krvi koja perzistira najmanje tri mjeseca i klinički je neobjašnjiva. Ključni je imunofenotip prisutnih stanica koji se manifestira koekspresijom B-limfocita na CD5, CD23 i CD19. U liječenju CLL prognostički faktori imaju značajnu ulogu u određivanju individualne terapije. Glavni prognostički markeri CLL su klinička faza bolesti, citogenetičke abnormalnosti, status IgHV mutacije gena za varijabilni region teških lanaca imunoglobulina (IgHV, engl. status of the tumor Ig heavy chain variable region genes), zeta asocirani protein od 70 kDa (ZAP-70, engl. Zeta-chain-associated protein kinase 70 i CD38 marker.

Cilj: Glavni cilj ovog istraživanja bio je uvođenje i standardizacija metode dokazivanja ekspresije ZAP-70 u stanicama pacijenata sa CLL primjenom protočne citometrije.

Materijali i metode: Ispitivanje je sprovedeno na 35 pacijenata čiji je uzorak upućen na analizu na protočnu citometriju radi postavljanja dijagnoze. Uputna dijagnoze je bila hronična limfatična leukemija

Rezultati: Primjenom protočne citometrije je utvrđeno da ekspresija proteina ZAP-70 dobro korelira sa prisustvom mutacije IgVH, mada su opisani i diskordantni slučajevi, a marker su slobodnog tretmana i preživljavanja. Kako se protočna citometrija rutinski koristi u dijagnozi CLL, određivanje ekspresije ZAP-70 protočnom citometrijom bio bi široko korišten prognostički marker. Uspješnost metode smo određivali utvrđivanjem korelacije između ekspresije ZAP-70 i prisustva ZAP-70 u T limfocitima i NK stanicama te korelacija sa genskim mutacijama pacijenata oboljelih od CLL.

Zaključak: Biće potreban daljnji rad za standardizaciju i imunofenotipsko određivanje ZAP-70. Jednostavnost protočne citometrije, koja se može koristiti za bilo kojeg novog pacijenta, zajedno sa rutinskim panelom dijagnostičkih testova, može pružiti moćan alat za prospektivne studije.

Ključne riječi: hronična limfatična leukemija, protočna citometrija, protein kinaza zap-70

INTRODUCTION

From historical point of view, the current classification of lymphoid neoplasms is based on the World Health Classification (WHO World Health Organization) from 2008. Previously known classifications are REAL - Revised European American Lymphoma and ILSG from 1994 - International Lymphoma Study Group. The REAL classification defined different entities taking into account the constellation between morphology, immunophenotype, genetic features, clinical picture and the course of disease development. The relative importance of each of these features is that they help distinguishing between different lymphoid neoplasms. However, there is no gold standard defining all diseases. Nevertheless, the lineage defines the characteristics of the cells and forms the

basis for the system structures classification, thus we distinguish B cell, T cell and killer cell (Natural killer - NK) neoplasms. In addition, the basic division of lymphoid neoplasms is into precursor lymphoid neoplasms and mature lymphatic neoplasm cells (1).

Neoplasms of mature lymphatic cells are also divided into neoplasms of B, T and NK lymphocyte or cell origin. The frequency and percentage of occurrence is certainly in favour of mature B lymphocytic neoplasms. Mature B lymphocyte neoplasms are broadly divided into small cell and large cell neoplasms. Small cell neoplasms include: chronic lymphatic leukemia (CLL), marginal zone lymphoma (MZL), mantle cell lymphoma (MCL), splenic marginal zone lymphoma (SMZL), hairy cell leukemia (HCL).

Chronic lymphocytic leukemia/small cell lymphoma CLL/SLL is a tumor of small, apparently mature lymphocytes that, in addition to pan B antibodies, also express CD5 and CD23 antibodies. Chronic lymphatic leukemia is by far the most common compared to mature B neoplasms.

Diagnostics and clinical classification

The scope of diagnostic tests in patients with suspected chronic lymphatic leukemia can differ from minimal to optimal and investigative. The usual diagnostic procedure includes a physical examination, hematological and biochemical laboratory tests, morphological analysis of peripheral blood, bone marrow, immunophenotyping, cytogenetic (karyotyping), molecular analysis and fluorescent in situ hybridization (FISH).

According to the International Workshop on Chronic Lymphocytic Leukemia - WCLL from 2008, the following criteria are needed for the chronic lymphocytic leukemia diagnosis:

- The number of lymphocytes in peripheral blood is higher than $5 \times 10^9/L$
- Conditionally even less if it is a chronic increase in the absolute number of lymphocytes with the morphological characteristics of chronic lymphocytic leukemia, the morphology

corresponds to small mature lymphocytes, without sails with phenotypic expression of one or more B cell markers (CD19, CD20, CD23), aberrant expression of CD5 and negative for other pan T cell markers.

The relationship between kappa and lambda confirms monoclonality. Lymphocytosis that persists for more than 3 months.

According to these criteria, a bone marrow biopsy is not required for diagnosis, but is still recommended to determine the cause and extent of bone marrow involvement (1).

Several classifications are used to determine the clinical stage of the disease. According to Rai and associates, among the oldest one is the classification from 1975, with 5 stages from 0-4. In addition, the Binet's classification from 1981 is also known, with 3 stages from A-C.

AIM

The aim of the study was to introduce and standardize the ZAP-70 expression method in CLL patients using flow cytometry.

MATERIALS AND METHODS

This was a fundamental and prospective study conducted in the period from 2014 to 2018. The research used bone marrow and peripheral blood samples from 35 newly diagnosed patients with a referral diagnosis of CLL. The analysis excluded patients who were already receiving therapy.

Determination of ZAP-70 and CD38 expression in bone marrow and peripheral blood samples from CLL patients was performed using flow cytometry. The presence of gene mutations in the cells of patients was determined by the cytogenetic FISH method (fluorescent *in situ* hybridization).

Peripheral blood and bone marrow samples submitted for immunophenotyping analysis were processed according to the protocol for preparing samples for flow cytometry analysis.

Bone marrow or peripheral blood is drawn into a vacutainer tube containing EDTA or lithium heparin. The sample is delivered to the laboratory within two hours. The entire panel of antibodies for the chronic lymphocytic leukemia diagnosis was performed according to Euroflow standards.

Bone marrow and peripheral blood samples sent for FISH analysis were processed according to the sample preparation protocol for fluorescent *in situ* hybridization and analysis on an interphase microscope with fluorescence filters.

The data obtained during the research conducted on a sample of thirty-five respondents were statistically processed and presented in tables and figures. The EXCEL program of functions and formulas was used for the results processing. A percentage ratio of the corresponding statistical data was made based on the obtained data.

RESULTS

The study included 35 patients from the Federation of Bosnia and Herzegovina and was conducted in the period from 15 December 2014 to

31 January 2018. The study was conducted on patients with a referral diagnosis of chronic lymphocytic leukemia (CLL).

The results of all analyzes serving as statistic basis are presented in Table 6 and Table 6.1. Based on gender, out of a total of 35 patients, 14 (40%) were female and 21 (60%) were male.

Patients were divided into age groups of 40-50, 50-60; 60-70; 70-80 and >80 years.

Based on the type of sample tested, patients were divided into two groups:

- patients with peripheral blood sample
- patients with bone marrow sample.

The study included 24 patients with bone marrow sample, and 11 patients with peripheral blood sample.

Analysed results

Table 1 and Table 1.1 contain the results of all the tests obtained in the study.

Table 1 Results of all tests conducted on 35 patients.

No .	CLL SCORE	CD19/ ZAP-70+	CD3/ ZAP-70+	NK/ ZAP-70+	CD19/ CD38 +	13q14.3	trisomy 12 centromere 12	17p13.1	13q.34 LAMP1	11q22.3	RAI
1	4/5	0	0	0	0	Normal	trisomy /abnormal	Normal	Disomy/normal	Weak signal	II
2	2/5	0	100%	0	11%	negative	negative	negative	negative	negative	0
3	5/5	0	100	0	17%	Normal	normal	Normal	Deletion /abnormal	Weak signal	IV
4	5/5	100	100	0	0	Normal	trisomy /abnormal	Normal	Normal	Normal	IV
5	5/5	83	100	0	0	Normal	normal	Normal	Normal	deletion/monosomy	IV
6	4/5	0	0	0	0	Normal	normal	Normal	Normal	Normal	II
7	5/5	1	80	100	0	Normal	normal	Normal	Normal	normal	II
8	3/5	0	100	100	0	negative	negative	negative	negative	Negative	II
9	5/5	1	0	0	0	Normal	normal	Normal	Normal	normal	I
10	5/5	0	0	0	0	Normal	normal	Indefinite	Normal	indefinite	I
11	5/5	0	0	0	0	Normal	normal	Normal	Normal	normal	I
12	4/5	0	0	0	0	negative	negative	negative	negative	negative	IV
13	5/5	0	100	1	0	Normal	trisomy/abnormal	Normal	Normal	normal	II
14	5/5	0	0	0	0	Normal	normal	Normal	Normal	normal	II
15	5/5	0	100	100	0	Normal	Trisomy/abnormal	Normal	Normal	normal	II
16	5/5	0	34	100	0	Weak signal	Weak signal	Normal	Normal	normal	IV

Table 1.1 Results of all tests conducted on 35 patients.

red br.	CLL SCO RE	CD19/ ZAP- 70+	CD3/ ZAP- 70+	NK/ ZAP- 70+	CD19/ CD38 +	13q14.3	trisomy 12 centrom ere 12	17p13.1	13q.34 LAMP1	11q22. 3	RAI
17	5/5	0	79	2	0	deletion/ab normal	Weak signal	Normal	Normal	normal	II
18	5/5	0	100	100	0	normal	normal	normal	normal	normal	II
19	3/5 S	0	85	100	0	negative	negative	negative	negative	negative	IV
20	5/5	0	100	100	0	normal	normal	normal	normal	normal	IV
21	5/5	0	100	100	0	normal	normal	normal	normal	normal	II
22	5/5	91	100	100	53	normal	normal	normal	normal	normal	IV
23	5/5	0	69	100	0	Weak signal	normal	normal	normal	normal	IV
24	3/5	0	78	100	16	negative	negative	negative	negative	negative	IV
25	3/5	0	100	100	0	Negative	negative	negative	negative	negative	IV
26	5/5	0	74	100	0	normal	normal	normal	normal	normal	I
27	5/5	0	0	0	0	normal	normal	normal	normal	normal	II
28	5/5	0	0	0	0	deletion/ab normal normal	normal	normal	normal	delecti on/abn ormal	II
29	5/5	0	94	0	0	No signal	normal	No signal	No signal	No signal	IV
30	5/5	0	0	0	0	deletion/ab normal normal	normal	normal	normal	deletio n/abno rmal	IV
31	5/5	0	100	0	0	deletion/ab normal normal	normala n	normalan	normala n	deletio n/abno rmal	II
32	5/5	0	100	0	0	No signal	trisomy/ abnorma l	normal	normal	normal an	III
33	5/5	0	100	0	0	normal	normal	normal	normal	normal	III
34	5/5	0	42	100	0	normal	normal	normal	normal	normal	II
35	5/5	0	32	100	0	normal	normal	normal	normal	deletio n/abno rmal	IV

DISCUSSION

Chronic lymphocytic leukemia is characterized by the gradual accumulation of malignant monoclonal CD5+ B lymphocytes in the bone marrow, peripheral

blood, lymph nodes, liver, and spleen. It is a disease characteristic of older people in the Western world and the Caucasian race, with a median onset above 61 years of age. One of the most interesting characteristics of the disease is its clinical

heterogeneity, from patients with rapid disease progression and early death to patients with a stable, non-progressive disease lasting for many years.

In 70% of elderly patient cases, chronic lymphatic leukemia is presented as asymptomatic or with mild symptoms and is most often discovered as a random finding of a blood test. Physical examination of the patient is mainly based on palpation of symmetrically enlarged regional lymph nodes. The main feature of the disease is lymphocytosis persistent for more than three months with a peripheral blood lymphocyte count higher than $5 \times 10^9/L$. Conditionally even less if it is a chronic increase in the absolute number of lymphocytes with the morphological characteristics of chronic lymphocytic leukemia, the morphology corresponds to small mature lymphocytes, without sails with phenotypic expression of one or more B cell markers (CD19, CD20, CD23), aberrant expression of CD5 and negative for other pan T cell markers. The diagnosis is based on the presence of the above criteria.

The clinical course of B chronic lymphocytic leukemia varies and new biological parameters should be added to the clinical parameters to predict an indolent or aggressive outcome of the disease. Therefore, it is very important to develop sensitive stratification parameters to identify patients with a poor prognosis.

Studies using DNA microarrays have shown that CLL cells have a characteristic gene expression profile in which the expression of a small subset of genes, including those encoding ZAP-70, IM1286077, and C-type lectin, correlates with the mutational status of the IgHV gene. ZAP-70, a member of the Syk-ZAP-70 protein tyrosine kinase family, is normally expressed in T lymphocytes and natural killer cells and plays a key role in initiating T-cell signaling. Recent studies have found that ZAP-70 is associated with enhanced cellular immunoglobulin receptor signaling in CLL B cells and that measurement of ZAP-70 can serve as a surrogate for IgHV mutational status. ZAP-70 protein can be conveniently measured by flow cytometry, unlike the technically demanding IgVH assay. In a larger series

of patients, Rassenti, et al., showed that ZAP-70 expression present in CLL cells is a more significant predictive factor for treatment than the IgVH gene. Moreover, ZAP-70 expression appears to be constant over time. CD38 expression has also been proposed as a surrogate marker for mutational status in B-CLL. Several studies have shown that high levels or density of CD38 expression on clonal lymphocytes is an unfavorable prognostic sign (2). Currently, both parameters are considered independent prognostic variables in B-CLL. Detection of CD38 expression on the cell surface can be easily performed by flow cytometry.

Genetic studies, using chromosomal analysis or interphase fluorescence *in situ* hybridization (FISH), have identified recurrent abnormalities with prognostic significance.

Patients with a normal karyotype or deletion of 13q14 as the only genetic abnormality have a better prognosis than those with a complex karyotype or deletion of 11q23 or 17p13. In large studies, these deletions have been associated with shorter overall survival.

Determining the course of the disease is best demonstrated by combining disease stage (Rai or Binet staging), with assessment of CD38 and ZAP-70 expression by flow cytometry, cytogenetics, and immunoglobulin V mutation status. Prognostic factors such as CD38, ZAP-70 and mutational analysis are particularly predictive when coincide.

The research was conducted on a sample of 35 patients treated at the Clinical Center University of Sarajevo with a referral diagnosis of chronic lymphatic leukemia/small lymphocyte lymphoma. The study analyzed bone marrow and peripheral blood samples. The study population comprised 24 patients (69%) with bone marrow sample, and 11 patients (31%) with peripheral blood sample.

Based on the age and gender of the total of 35 respondents, 21 were male and 14 were female. This confirms data from the literature indicating that men get sick more often than women, in a specific example there were 60% of sick men compared to

40% of sick women. The ratio of affected men and women was 1.5. It is also visible that the age distribution of patients confirms the literature thesis that CLL is a disease that occurs most often in people over 61 years of age.

In the studied population, not a single patient was between 40 and 50 years (0%), 6 of them were between 50 and 60 (17.1%), 12 between 60 and 70 (34.3%), 13 of them were between 70 and 80 (37.2%) and 4 of them were over 80 (11.4%). Given that the study showed that the median age of the examined patients was 13 (37.2%) at the age of 70-80 and a slightly smaller number of 12 patients (34.3%) at the age of 60-70, this sample is relatively close to the actual situation in the population. Both data, age and gender distribution, confirm the epidemiological theses of the disease (3).

As already stated, the diagnosis of CLL by flow cytometry is based on a series of parameters that include the phenotypic characteristics of the neoplastic clone and the use of CLL SCORE when interpreting the results (British Society of Hematology guidelines). CLL SCORE includes the combined positivity of B monoclonal lymphocytes CD19+ on CD23+ and CD5+, and negativity on CD79b, FMC7 and slg. In the study population, 27 patients (77.1%) had SCORE 5/5, 3 patients had SCORE 4/5 (8.6%), 4 patients (11.4%) had SCORE 3/5 and 1 patient had SCORE 2/5 (2.9%).

The results show that in the studied population, typical chronic lymphatic leukemia was diagnosed in 27 patients, atypical chronic lymphatic leukemia in 3 patients, Mantle cell lymphoma in 4 patients and another form of small cell lymphoma in 1 patient.

According to the clinical stage of Rai disease (4), in the study population 1 patient had stage 0 (2.9%), 4 had stage I (11.4%), 14 patients had stage II (40%), 2 patients had stage III (5.7%) and 14 patients had stage IV (40%) disease. Patients with a higher stage have a high risk, which determines the patient's further treatment. The higher the stage the more aggressive the therapy. Based on our results, it is evident that at the time of the examination, stage II and stage IV were equally represented (40%) in the

patients. Taking into account the main goal of the study, proving the expression of ZAP-70 in the cells of patients suffering from chronic lymphocytic leukemia, the selection of the sample preparation protocol was very important. The most important thing to emphasize is that ZAP-70 is an intracellular antibody, just like CD3, and for its correct binding to the cell or into the cell, initial holes must be made on the surface of the cell cytoplasm. Gibbs G, et al. (5) investigated the measurement of ZAP-70 expression in CLL using the Fix & Perm method of permeabilization and antibody binding as the easiest and the most sensitive and specific combination.

Therefore, this combination can provide a standardized flow cytometric method that can be introduced into routine CLL immunophenotypic analysis in the clinical diagnostic laboratory (6). For intracellular binding of antibodies, we used the sample preliminary lysing method with the original erythrocyte lysing buffer (FACS lysing solution 10x - BD). This buffer is also a cell membrane permeabilizer, which enables the binding of intracellular antibodies.

The study population included 25 patients (71.4%) in whom ZAP-70 appeared normally in CD3+ T lymphocytes, 15 patients (42.9%) in whom ZAP-70 appeared normally in CD3+ T lymphocytes and NK cells, and 3 patients (8.6%) in whom ZAP-70 expression occurred in CD19+ B monoclonal lymphocytes. Out of a total of 3 patients who had ZAP-70 expression in B lymphocytes, two patients (5.7%) also had ZAP-70 expression in CD3+ T lymphocytes. Only one patient (2.9%) had ZAP-70 expression in B monoclonal lymphocytes and also in CD3+ T lymphocytes and NK cells. In ten patients (28.6%), the expression of ZAP-70 in lymphocytes was not demonstrated.

In 3 patients from the total examined population, the expression of ZAP-70 in monoclonal B lymphocytes was proven, which was confirmed as correct by a positive internal control on CD3+T lymphocytes and/or NK cells. Based on the literature data (7), ZAP-70 occurs in about 30-40% of patients suffering from chronic lymphocytic leukemia. The obtained results are generally promising, but due to

the small sample, they are poorly comparable with other known studies and they lack statistical significance.

Given that in more than a quarter of patients, the result of proving the expression of ZAP-70 was negative in all lymphocytes (internal control and monoclonal lymphocytes), it can be concluded that this sample preparation method was relatively reliable and that a larger number of patients should be included and the method should be updated.

Although data from the literature indicate a certain degree of variability in the expression of ZAP-70 over time, prognostic predictions of the diagnosis do not change in majority of cases. Further analysis and standardization of the ZAP-70 preparation and analysis protocol on flow cytometry is certainly needed to solve the standardization problem (8).

Another prognostic factor that was examined in this study was the expression of Cyclic ADP ribose hydrolase CD38, which was also an important prognostic marker in chronic lymphocytic leukemia and indicated a poor prognosis (9). In the study population, four patients (11.4%) had expression of CD38 antibodies in B monoclonal lymphocytes. Specifically, 3 patients had CD38 expression in monoclonal B lymphocytes $\geq 30\%$ and one patient had CD38 expression in monoclonal B lymphocytes $<30\%$. In the remaining 31 (88.6%) patients, expression of CD38 antibodies in B monoclonal lymphocytes was not demonstrated. In only one patient (2.9%) the prognostic factors ZAP-70 and CD38 were expressed in parallel. That was a patient with normal expression of ZAP70+ in CD3-T lymphocytes and normal in NK cells (positive internal control) (10), and it could be stated that this patient had a reliable expression of ZAP-70 in correlation with the CD38 antibody. Given that this was one of the three patients with proven ZAP-70 expression, this patient actually represented one third (33.3%) of the samples with both unfavorable prognostic factors proven. The examination of the correlation between selected adverse prognostic factors in this study was statistically significant.

A correlation was found between ZAP-70 and CD38 expression regardless of the cut-off point taken for CD38 positivity, although the two markers did not identify the same group of patients. Although practically all patients with ZAP-70-positive CLL were positive for CD38 in many studies (11) in our work, only a third of patients with ZAP-70-positive CLL were positive for CD38 expression. An open question still remains as to what the result would be after a longer median follow-up and the inclusion of a significantly larger number of patients. The correlation between ZAP-70 expression and specific cytogenetic abnormalities was shown to be significant. Data related to the frequency of trisomy 12, del (6q), 11q22.3 or undetectable abnormalities in patients with ZAP-70-positive CLL correspond to previous results reported by Wiestner A, et al. (12).

Out of the total number of the examined patients, 17 (48.6%) had completely normal results of all FISH tests, 6 patients (17.15%) had negative results, and 12 patients (34.3%) had a result of some cytogenetic abnormality.

Analyzing each individual genetic analysis of FISH, according to the way of interpreting the results, we come to the following findings: when examining the gene abnormality of deletion 13q14.3, 25 patients (71.4%) had a normal finding, 6 patients (17.2%) had a negative finding, 4 patients (11.4%) had a deletion/abnormal finding.

When testing for the genetic abnormality trisomy 12, 24 patients (68.6%) had normal results, 6 patients (17.25%) had negative results, and 5 patients (14.3%) had trisomy/abnormal results. When testing for the genetic abnormality 17p13.1 deletion, 29 patients (82.8%) had normal findings, 6 patients (17.2%) and we had no patients (0%) with trisomy/abnormal findings.

When testing for the 13q34 LAMP1 deletion gene abnormality, 27 patients (77.1%) had normal results, 6 patients (17.2%) had negative results, and 2 patients (5.7%) had deletions/abnormal results.

When testing for the 11q22.3 deletion genetic abnormality, 24 patients (68.6%) had normal results,

6 patients (17.25%) had negative results, and 5 patients (14.3%) had trisomy/abnormal results.

And finally, taking into account the expression of ZAP-70 protein as a prognostic factor and genetic abnormalities, we made a correlation of these variables. Although a small number of the examined patients had ZAP-70 expression in CLL (3 patients), it should be taken into account that two-thirds of the total number of positive patients had a genetic abnormality.

Out of the total of three patients with proven chronic lymphocytic leukemia (8.6%) in whom ZAP-70 protein expression occurred in monoclonal B lymphocytes, two patients (5.7%) had proven genetic abnormality (one with trisomy 12 and the other with a deletion of 11q22.3), while one patient (2.9%) had normal cytogenetic analysis findings. In contrast, we found no association between ZAP-70 expression and del(17p).

This result is unexpected because many studies have shown that this is a high-risk genomic aberration occurring almost exclusively in patients with ZAP-70 positive status (13).

However, in other statistical reports, the presence of ZAP-70 is associated with del(11q) but not with del(17p) (14).

CONCLUSION

Using the sample preparation method we used in this study, out of a total of 35 patients examined, we demonstrated the normal presence of ZAP-70 antibodies in CD3+ T-lymphocytes as an internal control in the examined sample in 25 of them (71.4%). Overall, the results obtained are promising, but due to the small samples, further analysis and standardization of the ZAP-70 preparation and analysis protocol on flow cytometry is needed to resolve the standardization issue. In 3 patients with confirmed chronic lymphocytic leukemia, we proved the expression of ZAP-70 in monoclonal B lymphocytes and confirmed the reliability of ZAP-70 expression by its presence in the internal control. However, for correlation with large world studies, it is necessary to analyze a larger number of samples in

order to gain statistical significance, as well as to perform a correlation with IgVH mutation in order to one hundred percent complete the protocols with prognostic factors for chronic lymphatic leukemia. In one patient, we demonstrated the parallel expression of ZAP-70 protein with the presence of the expression of cyclic ADP ribose hydrolase CD38. In patients with ZAP-70 expression in monoclonal B lymphocytes, we proved the association with cytogenetic abnormalities. ZAP-70 and CD38 as a prognostic factor detected by flow cytometry have a complementary role in identifying patients requiring treatment. Comprehensive characterization of biological markers in prospective studies encourages to fully establishing the position of ZAP-70 in the prognostic algorithm of patients with CLL for progression, survival and response to treatment. Further work will be required for standardization and immunophenotyping of ZAP-70. The simplicity of flow cytometry, which can be used for any new patient, together with a routine panel of diagnostic tests, can provide a powerful tool for prospective studies.

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Authors' Contributions: AO and NB contributed significantly to the conception and design of the article, as well as the acquisition, analysis, and interpretation of data for the work. Each author had a role in drafting of the article and the revision process. Each author gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial Support and Sponsorship: nil.

Conflict of Interest: there are no conflicts of interest.

Characteristics and Causes of Intensified Hyperbilirubinemia in Term Neonates Hospitalized at the Department of Neonatology and the Neonatal Intensive Care Unit of the Clinical Center University of Sarajevo

Obilježja i uzroci intenzivirane hiperbilirubinemije kod terminske novorođenčadi hospitalizirane na Odjelu neonatologije i Jedinici neonatalne intenzivne njege Kliničkog centra Univerziteta u Sarajevu

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ABSTRACT

Introduction: Hyperbilirubinemia represents one of the most common clinical conditions in the neonatal period, especially in term neonates. It is estimated that it occurs in approximately 60-80% of newborns during the first days of life, while clinically significant forms, which require medical intervention, develop in about 8-10% of cases. The development of hyperbilirubinemia is associated with physiological and pathological factors, including increased production of bilirubin, immaturity of liver enzymes and enhanced enterohepatic circulation. The most important risk factors include low birth weight, exclusive breastfeeding (especially when associated with insufficient intake), gestational age at the lower limit of term, neonatal infections (including sepsis), maternal diabetes, and certain ethnic predispositions. Recent studies also highlight the role of genetic factors (e.g. UGT1A1 polymorphisms) and perinatal influences.

Aim: to analyze the clinical characteristics of intensified hyperbilirubinemia in term neonates and assess the possible influence of body weight loss, mode of delivery and gestational age on its occurrence.

Materials and methods: A retrospective clinical study was conducted by analyzing medical records of neonates hospitalized at the Department of Neonatology and Neonatal Intensive Care Unit of the Pediatric Clinic, Clinical Center University of Sarajevo (CCUS). The study included a total of 50 term neonates treated for hyperbilirubinemia in the period from 1 June 2021 to 31 January 2022. The examined population consisted of 54% male and 46% female neonates, with an average gestational age of 39 weeks. Most deliveries were performed vaginally. The average age of mothers was 33 years. The average duration of hospitalization was three days, and phototherapy was the most commonly

applied therapeutic method, in accordance with modern neonatal guidelines.

Results: showed a seasonal variation in the occurrence of intensified hyperbilirubinemia, with a higher incidence during autumn and lower during winter. No statistically significant association was found between gestational age and serum bilirubin levels, or between postnatal body weight loss and bilirubin values.

Conclusion: Intensified hyperbilirubinemia in term neonates remains a significant clinical challenge. However, no clear association was established with certain perinatal factors such as gestational age and postnatal body weight loss. Early identification of risk factors and adequate monitoring of newborns are key factors for the prevention of complications, including bilirubin encephalopathy.

Keywords: neonatal hyperbilirubinemia, phototherapy, neonatal care, bilirubin encephalopathy

SAŽETAK

Uvod: Hiperbilirubinemija predstavlja jedno od najčešćih kliničkih stanja u neonatalnom periodu, posebno kod terminskih novorođenčadi. Procjenjuje se da se javlja u približno 60-80% novorođenčadi tokom prvih dana života, dok se klinički značajne forme, koje zahtijevaju medicinsku intervenciju, razvijaju u oko 8-10% slučajeva. Nastanak hiperbilirubinemije povezan je sa fiziološkim i patološkim faktorima, uključujući povećanu proizvodnju bilirubina, nezrelost jetrenih enzima i pojačanu enterohepatičnu cirkulaciju. Najvažniji faktori rizika uključuju nisku porođajnu masu, ekskluzivno dojenje (posebno kada je povezano sa nedovoljnim unosom), gestacijsku dob na donjoj granici termina, neonatalne infekcije (uključujući sepsu), maternali dijabetes, te određene etničke predispozicije. Recentna istraživanja također ističu ulogu genetskih faktora (npr. polimorfizmi UGT1A1) i perinatalnih utjecaja.

Cilj: analizirati kliničke karakteristike intenzivirane hiperbilirubinemije kod terminskih novorođenčadi i procijeniti mogući utjecaj gubitka tjelesne mase, načina poroda i gestacijske dobi na njen nastanak.

Materijali i metode: Retrospektivna klinička studija provedena je analizom medicinskih kartona novorođenčadi hospitalizirane na Odjelu neonatologije i Neonatalne intenzivne njege Pedijatrijske klinike Kliničkog centra Univerziteta u Sarajevu. U istraživanje je uključeno ukupno 50 terminskih novorođenčadi liječene zbog hiperbilirubinemije u periodu od 1. juna 2021. do 31. januara 2022. Ispitana populacija sastojala se od 54% muške i 46% ženske novorođenčadi, sa prosječnom gestacijskom dobi od 39 sedmica. Većina poroda izvedena je vaginalno. Prosječna starost majki bila je 33 godine. Prosječno trajanje hospitalizacije bilo je tri dana, a fototerapija je bila najčešće primijenjena terapijska metoda, u skladu sa savremenim neonatalnim smjernicama.

Rezultati: su pokazali sezonsku varijaciju u pojavi intenzivirane hiperbilirubinemije, s većom incidencijom tokom jeseni i nižom tokom zime. Nije pronađena statistički značajna povezanost između gestacijske dobi i nivoa bilirubina u serumu, niti između postnatalnog gubitka tjelesne mase i vrijednosti bilirubina.

Zaključak: Intenzivirana hiperbilirubinemija kod terminskih novorođenčadi ostaje značajan klinički izazov; međutim, nije utvrđena jasna povezanost sa određenim perinatalnim faktorima kao što su gestacijska dob i postnatalni gubitak tjelesne mase. Rana identifikacija faktora rizika i adekvatno praćenje novorođenčadi su ključni za prevenciju komplikacija, uključujući bilirubinsku encefalopatiju.

Ključne riječi: neonatalna hiperbilirubinemija, fototerapija, neonatalna njega, bilirubinska encefalopatija

INTRODUCTION

Neonatal hyperbilirubinemia represents a significant clinical concern due to its high prevalence and possible complications. Approximately 60% of

term and up to 80% of preterm neonates develop visible jaundice during the first week of life. This condition arises from a combination of increased bilirubin production, immature liver metabolism and enhanced enterohepatic circulation (1,2).

Although physiological jaundice is usually self-limiting, certain cases progress to severe hyperbilirubinemia, which can lead to bilirubin neurological dysfunction, including acute bilirubin encephalopathy and kernicterus (3,4).

The trend toward early discharge from maternity wards increases the importance of identifying newborns at risk before the peak of bilirubin occurs. Proposed predictors include gestational age, adequacy of feeding, body weight loss and mode of delivery. However, available evidence remains inconsistent (5,6).

AIM

The aim of this study was to contribute to the understanding of intensified hyperbilirubinemia by analyzing clinical characteristics and assessing possible risk factors in term neonates (7).

MATERIALS AND METHODS

Study design

The study was designed as a retrospective, analytical, cross-sectional study and was conducted at the Department of Neonatology and Neonatal Intensive Care Unit of the Pediatric Clinic, Clinical Center University of Sarajevo. A total of 50 term neonates (≥ 37 weeks of gestation) hospitalized due to hyperbilirubinemia were included in the study.

Inclusion criteria

- Term neonates (≥ 37 weeks of gestation)
- Total serum bilirubin ≥ 255 $\mu\text{mol/L}$

Exclusion criteria

- Preterm neonates
- Congenital anomalies
- Neonatal infections

Data collection

Data were collected from medical records and included: demographic characteristics (sex, age), maternal characteristics (age), perinatal data (gestational age, mode of delivery), clinical parameters (birth weight, weight at admission), laboratory values (TSB levels), therapeutic methods (phototherapy), duration of hospitalization and season of birth

Statistical analysis

Statistical analysis was performed using MedCalc software. Descriptive statistics were presented as mean $\pm$ standard deviation or median (range). Analytical tests included: Chi-square test, Student's t-test and ANOVA. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Demographic and perinatal characteristics

The study included 50 term neonates, of which 54% were male and 46% female. The average gestational age was 39 weeks (range 37-41), while the average age of mothers was 33 ± 5.5 years. Most deliveries were vaginal (90%), while 10% were performed by caesarean section, with a statistically significant difference ($p < 0.05$).

Anthropometric data

The average birth weight was 3534 ± 451 g, while the average weight at admission was 3370 ± 448 g. A decrease in body weight was observed, but the difference was not statistically significant ($p = 0.071$).

Therapy and hospitalization

Phototherapy was applied in 96% of neonates, confirming its central role in the treatment ($p < 0.05$). The median duration of hospitalization was 3 days.

Seasonal distribution

The highest incidence of intensified hyperbilirubinemia was recorded in autumn (46%), followed by summer (28%), spring (14%) and winter (12%), with a statistically significant difference ($p < 0.05$).

Analysis of associations

No statistically significant association was found between: bilirubin levels and body weight loss $>10\%$ ($p = 0.612$) and bilirubin levels and gestational age ($p = 0.123$).

Table 1 Demographic Characteristics of Term Neonates.

Variable	Value
Total number	50
Male, n (%)	27 (54%)
Female, n (%)	23 (46%)

Table 2 Gestational Age and Maternal Age.

Variable	Mean $\pm$ SD	Range
Gestational age (weeks)	39.0 $\pm$ 1.2*	37–41
Maternal age (years)	33.0 $\pm$ 5.5	—

Table 3 Mode of Delivery.

Mode of delivery	n (%)
Vaginal delivery	45 (90%)
Cesarean section	5 (10%)

Table 4 Anthropometric Parameters.

Variable	Mean $\pm$ SD	p-value
Birth weight (g)	3534 $\pm$ 451	—
Weight at admission (g)	3370 $\pm$ 448	0.071

Table 5 Weight Loss.

Variable	Value
Mean weight loss (g)	164 g
Weight loss (%)	~4.6%

Table 6 Therapy.

Treatment	n (%)
Phototherapy	48 (96%)
No phototherapy	2 (4%)

Table 7 Length of Hospital Stay.

Variable	Median (Range)
Length of stay (days)	3

Table 8 Seasonal Distribution.

Season	n (%)
Autumn	23 (46%)
Summer	14 (28%)
Spring	7 (14%)
Winter	6 (12%)

Table 9 Association Analysis.

Variable	p-value	Interpretation
Bilirubin vs. weight loss $>10\%$	0.612	Not significant
Bilirubin vs. gestational age	0.123	Not significant

DISCUSSION

This study confirms that neonatal hyperbilirubinemia remains very common in term neonates, primarily within the expected range of gestational age (8,9).

One of the key findings is the absence of a statistically significant relationship between excessive body weight loss ($>10\%$) and elevated bilirubin levels (10,11). Although previous studies

suggest that inadequate feeding and dehydration may increase enterohepatic circulation of bilirubin, our results indicate that this relationship may not be simple (12).

Similarly, gestational age within the term range did not significantly influence bilirubin levels, suggesting that differences in maturity between 37 and 41 weeks may not be clinically relevant predictors in this context (13).

The observed seasonal variation, with a higher incidence in autumn, differs from some reports that indicate a higher frequency during warmer months. This difference may be explained by regional environmental factors, differences in neonatal care or breastfeeding patterns (14,15).

The high rate of phototherapy use in this study is consistent with modern clinical guidelines, emphasizing its role as the first-line treatment of neonatal hyperbilirubinemia (16,17). The relatively short duration of hospitalization further confirms its effectiveness and safety (18).

Overall, the results suggest that intensified hyperbilirubinemia is multifactorial, influenced by a complex interaction of physiological and environmental factors, rather than isolated predictors

CONCLUSION

Intensified hyperbilirubinemia is a common clinical occurrence in term neonates. This study did not find a significant association between bilirubin levels and body weight loss greater than 10% or gestational age. The results indicate that neonatal hyperbilirubinemia is a multifactorial condition that requires comprehensive clinical assessment. Phototherapy remains the cornerstone of treatment. Future prospective, multicenter studies are needed to better identify predictive factors and optimize early management strategies.

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- Authors' contributions:** ĐŠ, AR, FI, LJ and AH gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Financial support and sponsorship:** nil.
- Conflict of interest:** there are no conflicts of interest.

Diagnostic Value of CRP, Rheumatoid Factor and Anti -CCP Antibodies in Patients with Rheumatoid Arthritis

Dijagnostička vrijednost CRP, reumatoidnog faktora i anti -CCP antitijela kod pacijenata s reumatoidnim artritisom

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by systemic inflammation and progressive joint damage. Laboratory biomarkers are essential for early diagnosis and monitoring, but individual markers have limited diagnostic performance, highlighting the importance of their combined use.

Aim: to evaluate the diagnostic value of C-reactive protein (CRP), rheumatoid factor (RF), and anti-cyclic citrullinated peptide (anti-CCP) antibodies in patients with rheumatoid arthritis and to assess their complementary roles in clinical practice.

Materials and methods: This observational analytical study included 110 participants: 80 patients with rheumatoid arthritis and 30 healthy controls aged 35–55 years. CRP and RF levels were determined using immunochemical nephelometric methods, while anti-CCP antibodies were measured by ELISA. Descriptive statistics and Spearman correlation analysis were applied, with statistical significance set at $p < 0.05$.

Results: Significantly higher levels of CRP, RF, and anti-CCP antibodies were observed in patients with RA compared to controls. CRP reflected inflammatory activity, while RF and anti-CCP antibodies indicated autoimmune processes. Anti-CCP antibodies demonstrated the highest specificity, whereas RF showed moderate sensitivity but lower specificity. A significant positive correlation was found between RF and anti-CCP antibodies, while CRP did not correlate with autoantibodies.

Conclusion: The combined use of CRP, RF, and anti-CCP antibodies improves diagnostic accuracy in rheumatoid arthritis. Anti-CCP antibodies are particularly valuable for early diagnosis and prognostic assessment, while CRP remains essential for evaluating inflammatory activity.

Keywords: rheumatoid arthritis, CRP, rheumatoid factor, anti-CCP, biomarkers

SAŽETAK

Uvod: Reumatoidni artritis (RA) je hronična autoimuna bolest karakterizirana sistemskom

upalom i progresivnim oštećenjem zglobova. Laboratorijski biomarkeri imaju ključnu ulogu u ranoj dijagnostici i praćenju bolesti, ali pojedinačni markeri imaju ograničenu dijagnostičku vrijednost, zbog čega je važna njihova kombinovana primjena.

Cilj: ispitati dijagnostički značaj C-reaktivnog proteina (CRP), reumatoidnog faktora (RF) i anti-CCP antitijela kod pacijenata s reumatoidnim artritisom, te procijeniti njihov komplementarni značaj u kliničkoj praksi.

Materijali i metode: Istraživanje je obuhvatilo 110 ispitanika: 80 pacijenata s reumatoidnim artritisom i 30 zdravih kontrola starosti 35–55 godina. Koncentracije CRP i RF određivane su imunohemijskim metodama na nefelometru, dok su anti-CCP antitijela određivana ELISA metodom. Korištene su deskriptivne statističke metode i Spearmanova korelacijska analiza, uz nivo statističke značajnosti $p < 0,05$.

Rezultati: Kod pacijenata s RA utvrđene su značajno više vrijednosti CRP, RF i anti-CCP antitijela u odnosu na kontrolnu grupu. CRP odražava inflamatornu aktivnost, dok RF i anti-CCP ukazuju na autoimune procese. Anti-CCP antitijela pokazala su najveću specifičnost, dok RF ima umjerenu osjetljivost uz nižu specifičnost. Uočena je značajna pozitivna korelacija između RF i anti-CCP antitijela, dok CRP nije pokazao korelaciju s autoantitijelima.

Zaključak: Kombinovana primjena CRP, RF i anti-CCP antitijela značajno poboljšava dijagnostičku tačnost kod reumatoidnog artritisa. Anti-CCP antitijela imaju posebnu vrijednost u ranoj dijagnozi i procjeni prognoze, dok CRP ostaje ključni marker inflamatorne aktivnosti.

Ključne riječi: reumatoidni artritis, CRP, reumatoidni faktor, anti-CCP, biomarkeri

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease affecting approximately 0.5–1% of the adult population, with a higher prevalence among women (1,2). It is characterized by persistent

synovial inflammation, progressive joint destruction, and systemic manifestations that may significantly impair quality of life (3).

The pathogenesis of RA is complex and involves an interplay between genetic susceptibility, environmental triggers, and immune dysregulation (4,5). Both innate and adaptive immune responses contribute to disease development, including activation of autoreactive B and T lymphocytes, production of autoantibodies, and formation of immune complexes (5,6).

Serological biomarkers play a central role in the diagnosis and monitoring of RA. Rheumatoid factor (RF), one of the earliest described markers, has moderate sensitivity but limited specificity, as it may be present in other autoimmune and infectious diseases (7,8). In contrast, anti-cyclic citrullinated peptide (anti-CCP) antibodies demonstrate high specificity and are associated with early disease, radiographic progression, and unfavorable outcomes (9-11).

C-reactive protein (CRP), an acute-phase reactant synthesized in response to inflammatory cytokines such as interleukin-6, reflects systemic inflammatory activity and is widely used to assess disease activity and therapeutic response (12,13).

Given the heterogeneity of RA and the limitations of individual biomarkers, a combined diagnostic approach is recommended and incorporated into current classification criteria (14,15).

AIM

The aim of the study was to evaluate the diagnostic value of CRP, RF, and anti-CCP antibodies in patients with rheumatoid arthritis and to assess their complementary roles in clinical practice.

MATERIALS AND METHODS

This observational analytical study was conducted at the Department of Clinical Immunology, Clinical Center University of Sarajevo, during 2016.

The study included a total of 110 participants: 80 patients diagnosed with rheumatoid arthritis and 30 healthy individuals serving as a control group. All participants were between 35 and 55 years of age. The diagnosis of RA was established based on clinical and laboratory criteria, while control subjects had no history of autoimmune or inflammatory diseases.

Blood samples were obtained by venipuncture under standard aseptic conditions. Serum was separated by centrifugation and used for further laboratory analyses. All samples were processed and stored in accordance with standard laboratory protocols.

CRP and RF concentrations were measured using immunochemical methods on a nephelometric analyzer (BN II). Anti-CCP antibodies were determined using enzyme-linked immunosorbent assay (ELISA), with absorbance measured at 450 nm, according to the manufacturer's instructions.

Descriptive statistical methods were applied, including calculation of mean values, standard deviation, and range (minimum–maximum). Spearman correlation analysis was used to assess relationships between variables. Statistical significance was defined as $p < 0.05$.

The study was conducted in accordance with ethical standards for biomedical research.

RESULTS

The study included 80 patients with rheumatoid arthritis and 30 healthy controls. Laboratory findings demonstrated clear differences between the groups, reflecting both inflammatory activity and autoimmune processes in RA.

CRP levels were elevated in the majority of patients, with a mean value of 23.72 ± 29.35 mg/L, indicating active systemic inflammation and variability in disease activity.

Rheumatoid factor (RF) was increased in most patients (mean 279.64 ± 337.46 IU/mL), showing

considerable variability, which reflects heterogeneity in immune response and disease severity.

Anti-CCP antibodies were detected in a high proportion of patients (mean 5.88 ± 4.46 RU/mL), with a more consistent distribution compared to RF, supporting their specificity for RA (Table 1).

Table 1 Values of the Analyzed Parameters in the Study Group.

Analyzed parameters (N=80)	CRP(mg/L)	RF(IU/ml)	CCP(RU/ml)
The Mean value	23.72	279.64	5.88
Standard deviation	29.35	337.46	4.46
Minimum value	1.15	7.90	0.26
Maximum value	215	1970	20.54
Coefficient of variation	1.24	1.21	0.76
Deviations From Normal Distribution	4.12	2.65	0.35
Kurtosis	22.85	9.70	-0.50

Table 2 Results of Spearman's Correlation Coefficient.

Variable	CRP (mg/L)	RF (IU/mL)	CCP (RU/mL)
CRP (mg/L)	1.000	0.029	-0.196
<i>p-value</i>	—	0.796	0.081
RF (IU/mL)	0.029	1.000	0.252*
<i>p-value</i>	0.796	—	0.024
CCP (RU/mL)	-0.196	0.252*	1.000
<i>p-value</i>	0.081	0.024	—

* Spearman’s rho is presented as the correlation coefficient; p < 0.05 is indicated by (*); N = 80

A statistically significant positive correlation was observed between RF and anti-CCP antibodies (p<0.05), while no significant correlation was found between CRP and CCP autoantibodies (Table 2).

Additionally, CRP was elevated in 87.5% of patients, RF was positive in 92.5%, and anti-CCP antibodies in 81.25% of patients, further supporting their diagnostic relevance (Table 3).

Table 3 Comparison of the Results of CRP, RF, and CCP Concentration Measurements Between the Control and the Study Group.

Parameters	Group	$\bar{X}$	T-test	p
CRP (mg/L)	Study group	23.72	1.990	p<0.001
	Control group	3.11		
RF (IU/ml)	Study group	279.64	1.990	p<0.001
	Control group	1.09		
CCP (RU/ml)	Study group	5.88	1.900	p<0.001
	Control group	0.07		

$\bar{X}$ - Arithmetic mean, t-value of Student’s t-test, p-value (empirical level of significance).

DISCUSSION

The high prevalence of RF (92.5%) observed in our cohort is consistent with previous studies reporting RF positivity in approximately 70-90% of patients with established RA (1,7). However, despite its relatively high sensitivity, RF lacks specificity, as it may be present in other autoimmune diseases, chronic infections, and even in healthy elderly populations (7,8).

Anti-CCP antibodies, detected in 81.25% of patients in our study, represent a highly specific

biomarker for RA. Numerous studies have demonstrated that anti-CCP antibodies have a specificity exceeding 95%, making them superior to RF in distinguishing RA from other inflammatory conditions (9,10). Furthermore, anti-CCP antibodies may be detectable several years before the onset of clinical symptoms, which supports their role in early diagnosis and disease prediction (16,17). Their presence has also been associated with more severe disease, radiographic progression, and poorer functional outcomes (9,11). The findings of our study are in agreement with these observations.

CRP, as an acute-phase reactant, reflects systemic inflammation rather than disease-specific immune processes. Elevated CRP levels were observed in 87.5% of patients. However, the lack of statistically significant correlation between CRP and autoantibodies (RF and anti-CCP) is expected, as CRP reflects cytokine-driven inflammation, whereas RF and anti-CCP represent adaptive immune mechanisms (12,18). Similar findings have been reported in previous studies, where CRP correlates more strongly with disease activity scores than with serological markers (8,19).

The significant correlation between RF and anti-CCP antibodies observed in this study suggests overlapping immunopathological mechanisms, particularly B-cell activation and autoantibody production (6,20).

From a clinical perspective, the combined use of these biomarkers offers the greatest diagnostic value. While anti-CCP provides high specificity and prognostic information, RF contributes to sensitivity, and CRP reflects inflammatory burden and disease activity (14,21). Current classification criteria for RA also emphasize the importance of combining serological and inflammatory markers (15).

The main limitation of this study is its cross-sectional design, which precludes assessment of temporal relationships and disease progression. Additionally, the relatively limited sample size may affect the generalizability of the results. Future studies should focus on longitudinal analysis and

integration of biomarkers into predictive models for personalized treatment strategies.

COUNCLUSION

This study confirms that serological biomarkers play a crucial role in the diagnosis and management of rheumatoid arthritis. Anti-CCP antibodies demonstrated the highest diagnostic specificity and are particularly valuable for early detection and prognostic assessment. Rheumatoid factor, although sensitive, lacks specificity and should be interpreted in combination with other markers. CRP remains an essential indicator of inflammatory activity and is useful for monitoring disease progression and therapeutic response, although it does not provide disease-specific diagnostic information. The combined use of CRP, RF, and anti-CCP antibodies significantly enhances diagnostic accuracy and provides a comprehensive assessment of disease status.

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Authors' Contributions: MŠ, NDž, EZ, AČ, SDž and SM contributed significantly to the conception and design of the article, as well as the acquisition, analysis, and interpretation of data for the work. Each author had a role in drafting of the article and the revision process. Each author gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial Support and Sponsorship: nil.

Conflict of Interest: there are no conflicts of interest.

Care and Treatment of Women Undergoing Medical Abortion

Njega i liječenje žena koje su podvrgnute medicinskom abortusu

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ABSTRACT

Introduction: Medical abortion is a safe and effective method for terminating early pregnancy using pharmacological agents. The role of healthcare professionals, especially nurses, is crucial in providing appropriate care, education, and psychological support to women.

Aim: to present the treatment process and the importance of nursing care in improving outcomes and quality of life. The methodology includes literature analysis and simulated research.

Materials and methods: Type of research: descriptive; population: women with medical abortion; method: survey and monitoring of symptoms and complications; instruments: tables, figures.

Results: indicate that proper education and continuous care significantly reduce complications and anxiety.

Conclusion: Medical abortion is a modern, safe and effective method for terminating early pregnancy, which plays a significant role in improving women's reproductive health

Keywords: medical abortion, nursing care, treatment, quality of life

SAŽETAK

Uvod: Medicinski abortus je sigurna i učinkovita metoda za prekid rane trudnoće korištenjem farmakoloških sredstava. Uloga zdravstvenih radnika, posebno medicinskih sestara, ključna je u pružanju odgovarajuće njege, edukacije i psihološke podrške ženama.

Cilj: predstaviti proces liječenja, kao i važnost medicinske njege u poboljšanju ishoda i kvalitete života žena. Metodologija uključuje analizu dostupne literature i simulirano istraživanje.

Materijali i metode: Vrsta istraživanja: deskriptivno; populacija: žene s medicinskim abortusom; metoda: anketa i praćenje simptoma i komplikacija; instrumenti: tabele, slike.

Rezultati: pokazuju da pravilna edukacija i kontinuirana njega značajno smanjuju komplikacije i anksioznost.

Zaključak: Medicinski abortus je moderna, sigurna i efikasna metoda za prekid rane trudnoće, koja igra značajnu ulogu u poboljšanju reproduktivnog zdravlja žena.

Ključne riječi: medicinski abortus, medicinska njega, kvalitet života, liječenje

INTRODUCTION

Medical abortion is a modern, safe and widely used method for terminating early pregnancy, performed by pharmacological means instead of surgical intervention. In recent decades, this method has gained importance in women's reproductive health, owing to its high efficiency, availability and less invasiveness. The most commonly used therapy involves a combination of Mifepristone and Misoprostol, which work synergistically to cause termination of pregnancy (1). The first drug blocks the action of progesterone - a hormone necessary for maintaining pregnancy, while the other one causes uterine contractions and the fetus expulsion (2). This method is usually used in the first trimester, most often up to 9-12 weeks of pregnancy. Medical abortion represents a significant advance in gynecological practice as it allows for greater autonomy and privacy for women. At the same time, it reduces the risk of complications associated with surgical procedures, such as infections, uterine injuries, and anesthetic risks. According to world health organizations, when performed according to protocol, this method has a high success rate and a low rate of serious complications. However, despite its safety, medical abortion requires careful medical supervision and appropriate health care. This is where the role of the nurse comes to the fore, as she has a key function in the process of preparation, monitoring and post-intervention care (3).

Medical care includes not only physical care, but also education, psychological support and counselling, which is especially important given that women often face emotional stress, fear and uncertainty. In addition, quality medical care plays a significant role in the early recognition and prevention of possible complications, such as heavy bleeding, infection, or incomplete abortion. With proper education, women are able to recognize alarming symptoms and seek medical help in a timely manner. This directly affects the improvement of outcomes and preservation of her health. In the modern healthcare system, emphasis is placed on a holistic approach to patient care, which means treating the woman as a whole - with her physical, psychological, and social needs. In that regard, the

nurse has an important role as an educator, supporter and mediator between the patient and the doctor (4). Medical abortion is a method of terminating a pregnancy using medication, without surgical intervention. It is a safe and effective alternative to surgical abortion.

The purpose of this paper is to present the principles of care and treatment of women with medical abortion, as well as to highlight the importance of the nurse's role in improving the quality of health care and the lives of patients.

Pharmacological treatment

The most commonly used combination is: Mifepristone and Misoprostol.

Mechanism of action: Mifepristone → blocks progesterone Misoprostol → causes contractions and expulsion (5).

Indications: early pregnancy (up to 12 weeks), medical reasons and personal choice (6).

Contraindications: ectopic pregnancy, chronic diseases and drug allergies.

Advantages of medical abortion: non-invasive method, greater privacy, lower risk of infections, and natural course.

Disadvantages: longer duration, pain and bleeding, and the possibility of incomplete abortion.

Complications: heavy bleeding, infection and retained products (7).

The role of the nurse

The nurse has a key role in the following:
Before the intervention: education and psychological support.
During treatment: monitoring vital signs and pain assessment.
Following the intervention: monitoring for complications and counseling.
Medical care for women undergoing medical abortion is a continuous and structured process

carried out in several stages: before the procedure, during the treatment and after its completion. The goal is to ensure safety, reduce the risk of complications and improve the physical and psychological condition of the patient.

Care before medical abortion

This phase is extremely important as it prepares the patient physically and mentally for the procedure.

Health assessment

The nurse participates in the following: taking a medical history (previous pregnancies, illnesses, allergies), checking gestational age and assessing risk factors. Special attention is paid to: anemia, coagulation disorders and chronic diseases.

Patient education

Education is a key component and includes an explanation of the medical abortion procedure, the use of Mifepristone and Misoprostol, expected symptoms (bleeding, pain), and the duration of the procedure. The patient should be informed about normal reactions and alarming symptoms.

Psychological support

Women often face: fear, anxiety and guilt.

The nurse should: show empathy, ensure confidential communication and encourage asking questions.

Preparation for the procedure: give informed consent, explain the course of the day and advise on the presence of an escort.

Care during medical abortion

This phase begins with the application of therapy and lasts until the process is completed.

Application of therapy: application of Mifepristone and Misoprostol after 24-48 hours

Nurse: monitors proper application and provides instructions for home use (if necessary).

Monitoring symptoms

The most common symptoms: vaginal bleeding, abdominal pain, cramps and nausea.

The nurse performs: assessment of pain intensity, monitoring of vital parameters, and assessment of bleeding volume

Pain control: counseling on analgesics, application of warm compresses, and relaxation techniques.

Recognizing complications

The nurse must recognize: profuse bleeding (more than 2 sanitary pads/hour), high fever and severe pain.

In such cases → emergency medical intervention

Care after medical abortion

This phase is crucial for recovery and prevention of complications.

Physical monitoring: assessment of bleeding, monitoring of general condition and check-up after 7–14 days.

Prevention of infections

Tips: maintaining personal hygiene, avoiding tampons and sexual intercourse for a certain period and monitoring symptoms (temperature, unpleasant odor).

Psychological support

Women can experience: sadness, relief and emotional changes.

Nurse: offers conversation and recommends counseling if necessary.

Contraception education: counseling on methods and prevention of unwanted pregnancy.

Assessment of success

Assessment: whether the abortion is complete and the need for additional intervention.

Holistic approach to care

Modern medical care is based on: individual approach, respect for privacy and cultural sensitivity. The nurse should see the patient as: a physical, psychological and social being.

The role of the nurse in improving the quality of life

Proper care results in: reduced complications, better information, psychological stability, and faster recovery.

Medical care for medical abortion is a complex process requiring expertise, empathy and continuous monitoring. Proper care significantly affects a woman's safety, outcome and quality of life.

AIM

The aim of the study was to examine the role of medical care in medical abortion, its impact on the physical and psychological condition of the woman, to analyze care before, during and after the procedure, monitor complications and their distribution, and to examine the impact of education and psychological support.

MATERIALS AND METHODS

The study was descriptive and included women with medical abortion. Method of research was a survey and monitoring of symptoms and complications. The study instruments were tables and figures.

RESULTS

Table 1 **Outcomes of Medical Abortion.**

Parameter	Percent (%)
Satisfaction with medical care	85%
Occurrence of complications	10%
The need for additional intervention	5%

Out of the total number of women included in the study, 85% expressed satisfaction with medical care, while 10% had certain complications. Only 5% needed additional medical intervention.

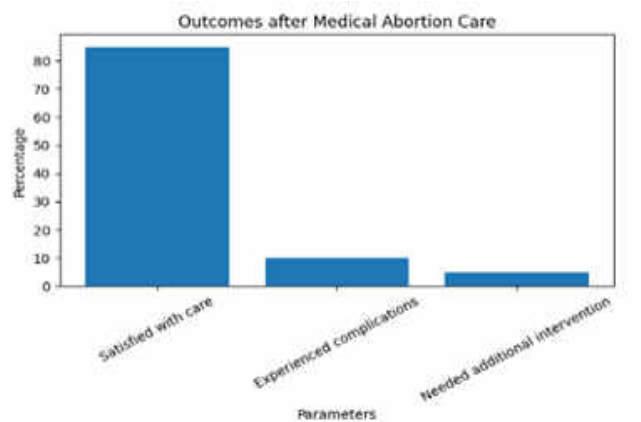


Figure 1 **Care Outcomes.**

High level of satisfaction and low complication rate.

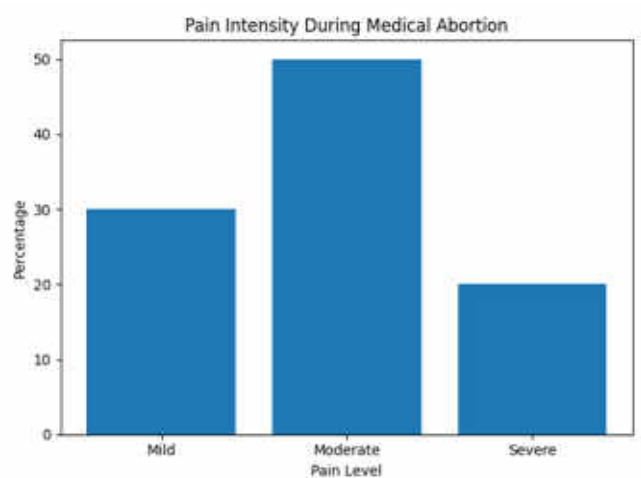


Figure 2 **Pain Intensity.**

The largest number of women (50%) reported moderate pain, 30% mild, and 20% severe pain.

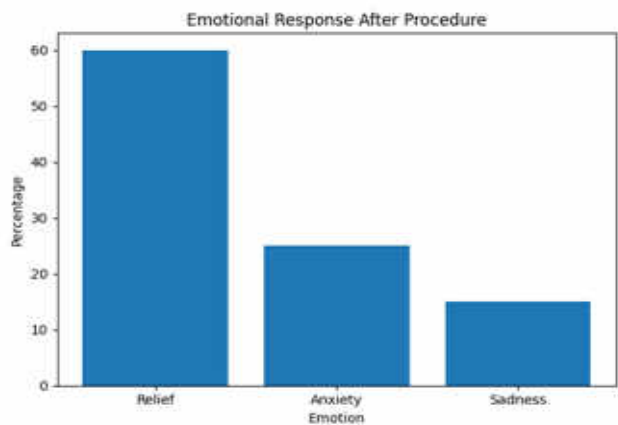


Figure 3 Emotional State.

The most common emotion was relief (60%), while some patients felt anxiety (25%) and sadness (15%).

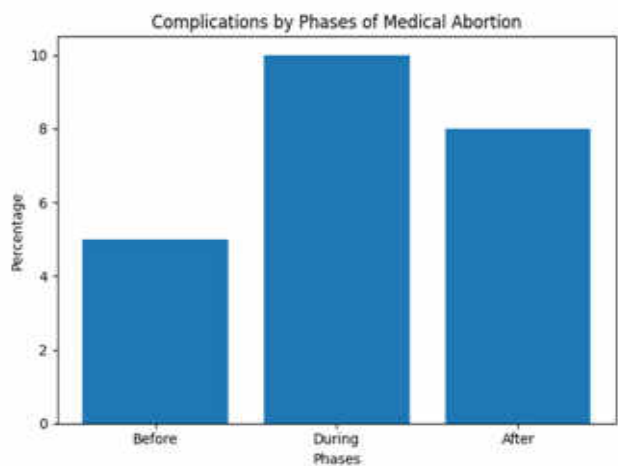


Figure 4 Complications by Phases: Before, During and after Medical Abortion.

Table 2 Level of Education.

Primary education	20%
Secondary education	50%
Highre education	30%

Majority of the respondents had secondary education (50%), while 30% had higher education, and 20% had primary education. This indicates that medical abortion was present among women of

different educational levels, but most often among those with secondary education.

Table 3 Number of Pregnancies.

1 pregnancy	45%
2 pregnancies	35%
3 or more pregnancies	20%

The highest percentage of women (45%) had a single pregnancy, indicating that medical abortion was often used in women in the early reproductive phase.

Table 4 Information before the Procedure.

Well informed	70%
Partially informed	20%
Uninformed	10%

Most patients were well informed before the procedure, which indicated the significant role of the nurse in education.

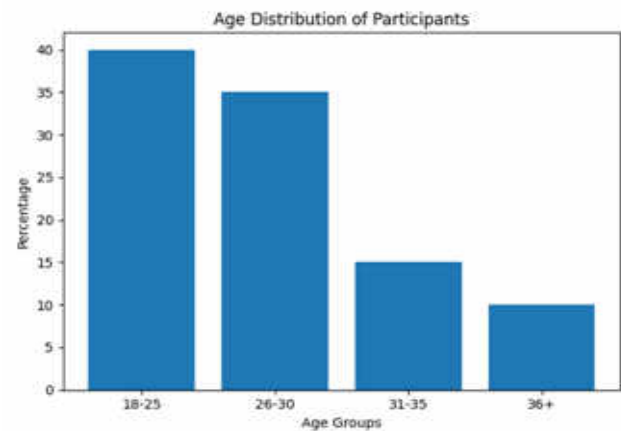


Figure 5 Age Structure.

The largest percentage of respondents was in the 18-25 (40%) age group, followed by 26-30 (35%) age group. Smaller numbers was in the 31-35 (15%) and 36 (10%) age groups.

The data indicate that medical abortion was most commonly used among younger women of reproductive age.

Clinical Study from the University Clinic in Skopje

A pilot study was conducted at the University Clinic of Gynecology and Obstetrics in Skopje, covering the results of medical abortion up to 22 weeks of gestational age.

The study included a total of 208 women. In the group up to 12 weeks, 168 women (97.1%) had a complete abortion. In the 12 to 22 week group, 25 women (71.4%) had a complete abortion. Acceptability of the method was high (95.14% in the first group and 82.14% in the second group).

The study indicates the high efficacy, safety and acceptability of medical abortion in this clinical setting.

Official reports by 2025 showed the following:

- In 2025, a total of 929 abortions up to 12 weeks of pregnancy were performed at the Department of Gynecology in Skopje.
- Out of this number, medical abortion was performed in 737 patients (86%) using pills.
- The remainder were surgical abortions (about 14%).
- There were also minor patients (the youngest was 15 years old) with medical abortion.

These data illustrate the practicality and actual application of the medical method in local clinical practice.

Table 5 Number of Abortions at the Gynecology Clinic in Skopje by Year (2022-2025).

Year	Total number of abortions	Medical abortions	Surgical abortions	% medical abortions
2022	880	745	135	84.7%
2023	910	780	130	85.7%
2024	945	815	130	86.2%
2025	929	737	192	79.4%

Table 6 Outcome of Medical Abortion by Gestational Age Groups.

Gestational age group	Number of women	Complete abortion	Failure/need for intervention	Completed in %
Up to 12 weeks	168	163	5	97.1%
12-22 weeks	35	25	10	71.4%

Table 7 Complications in the Skopje Clinical Hospital (2022–2025).

Year	Total medical abortions	Complications	Complications in %
2022	745	60	8.1%
2023	780	65	8.3%
2024	815	70	8.6%
2025	737	68	9.2%

During the 2022–2025 period, a slight increase in the percentage of complications associated with medical abortion was recorded (from 8.1% to 9.2%). That was mainly due to minor side effects such as

heavy bleeding or unnecessary intervention, but serious complications remained rare.

DISCUSSION

The results of the study show the significant role of medical care in the treatment of women with medical abortion. The analysis shows a high level of satisfaction among patients (85%), indicating that quality communication, education and continuous support have a direct impact on women's positive experience. These results are in line with the World Health Organization recommendations, emphasizing that properly organized health care and access to information significantly improve the outcome of medical abortion. According to their guidelines, informed patients and active participation in the process reduce anxiety and fear.

The complication rate in this study was 10%, which was within the expected values based on the literature. Studies show that medical abortion has a low rate of serious complications, especially when the combination of Mifepristone and Misoprostol is used.

This confirms the safety of the method, but at the same time emphasizes the need for careful monitoring of patients.

With regard to pain, the largest percentage of women (50%) reported moderate pain, which was expected considering the mechanism of action of the therapy. Pain is a result of uterine contractions and is an integral part of the process.

However, with appropriate medical intervention, such as counseling on analgesics and psychological support, this condition can be significantly alleviated. The emotional state of the patients shows that most of them feel relief (60%), but a significant percentage have anxiety (25%) and sadness (15%). This indicates that medical abortion is not only a physical, but also a psychological process. Therefore, the role of the nurse as a supporter and advisor is essential.

Furthermore, only 5% of patients needed additional intervention, which confirms the high efficiency of the method. This result is consistent with numerous studies indicating that the success rate of medical abortion is over 95%.

CONCLUSION

Medical abortion is a modern, safe and effective method for terminating early pregnancy, which plays a significant role in improving women's reproductive health. Based on the analysis of theoretical knowledge and the results obtained in the study, it can be concluded that medical care is of crucial importance in all phases of medical abortion - before, during and after the intervention. The results of the study showed a high level of patients' satisfaction, a low complication rate, and minimal need for additional interventions. Therefore, a holistic approach to medical care, encompassing a woman's emotional and social needs, is necessary for her overall health and well-being. It can be concluded that medical abortion, when accompanied by quality and individualized medical care, is a safe, effective, and humane approach to caring for women's reproductive health.

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Authors' contributions: ES, GK-M and GP gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial support and sponsorship: nil.

Conflict of interest: there are no conflicts of interest.

The Work Tasks of the Family Nurse in the Care, Treatment and Education of Postoperative Patients in the Municipality of Veles

Radni zadaci porodične medicinske sestre u njezi, liječenju i edukaciji postoperativnih pacijenata u Općini Veles

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ABSTRACT

Introduction: The postoperative period is an important phase in the patient's recovery after surgery, which requires continuous health care, proper care of the surgical wound, monitoring of the health condition, timely application of therapy and recognition of possible complications. After discharge from hospital treatment, the family nurse plays an important role in providing professional support in the home, as well as in connecting the patient, the family and the health system.

Aim: to analyze the work tasks of the family nurse in the care, treatment and education of postoperative patients in the Municipality of Veles.

Materials and methods: The research was quantitative and descriptive, using a structured questionnaire among 30 postoperative patients and 10 family nurses. The patients' experiences with home postoperative care, the education received the occurrence of complications and satisfaction with the health service, as well as the professional activities, challenges and competencies of family nurses will be examined.

Results: The analysis showed that regular nursing care and health education contribute to a safer

recovery, better information of patients and a reduction in the risk of postoperative complications.

Conclusion: The issue is important for the promotion of primary health care and for improving the quality of home care for postoperative patients.

Keywords: family nurse, postoperative care, treatment, education, home health care, postoperative complications, Municipality of Veles

SAŽETAK

Uvod: Postoperativni period je važna faza u oporavku pacijenta nakon operacije, koja zahtijeva kontinuiranu zdravstvenu njegu, pravilnu njegu operativne rane, praćenje zdravstvenog stanja, pravovremenu primjenu terapije i prepoznavanje mogućih komplikacija. Nakon otpusta sa bolničkog liječenja, porodična medicinska sestra igra važnu ulogu u pružanju stručne podrške u kući, kao i u povezivanju pacijenta, porodice i zdravstvenog sistema.

Cilj: analiza radnih zadataka porodične medicinske sestre u njezi, liječenju i edukaciji postoperativnih pacijenata u općini Veles. Istraživanje će biti kvantitativno i deskriptivno, korištenjem strukturiranog upitnika među 30

postoperativnih pacijenata i 10 porodičnih medicinskih sestara.

Materijali i metode: Ispitatana su iskustva pacijenata s kućnom postoperativnom njegom, primljena edukacija, pojava komplikacija i zadovoljstvo zdravstvenom uslugom, kao i profesionalne aktivnosti, izazovi i kompetencije porodičnih medicinskih sestara.

Rezultati: Analiza je pokazala da redovna medicinska njega i zdravstveno obrazovanje doprinose sigurnijem oporavku, boljoj informiranosti pacijenata i smanjenju rizika od postoperativnih komplikacija.

Zaključak: Ovo je važno za promociju primarne zdravstvene zaštite i za poboljšanje kvalitete kućne njege postoperativnih pacijenata.

Ključne riječi: porodična medicinska sestra, postoperativna njega, liječenje, edukacija, kućna zdravstvena njega, postoperativne komplikacije, općina Veles

INTRODUCTION

Modern health care increasingly emphasizes the need for continuing care, especially for patients continuing their recovery at home after surgery. The postoperative period does not end with discharge from hospital, but continues through monitoring, care, treatment and health education. During this phase, the patient may experience pain, limited mobility, fear, uncertainty, the need for assistance with daily activities, and the risk of complications, such as surgical wound infection, bleeding, swelling, thrombosis, or inadequate response to therapy.

The family nurse is an important member of the primary health care team. Her work is not limited to the technical performance of medical interventions, but it also includes assessing the patient's condition, planning and implementing nursing activities, health education, counseling, family support, and coordination with the family doctor and other healthcare professionals. She has direct insight into the life and treatment conditions of the patient,

which enables timely identification of risks and taking appropriate measures (1).

In postoperative patients, the work tasks of a family nurse most often relate to controlling and dressing the surgical wound, monitoring vital signs, assessing pain, administering prescribed therapy, monitoring possible adverse reactions, maintaining health records, and providing clear guidelines for home care.

The educational role is particularly important, as the patient and his family need to know how to properly maintain hygiene, when to seek medical help, how to take therapy and recognize symptoms that may indicate a complication (2).

The choice of topic is important given that quality postoperative care at home can contribute to faster and safer recovery, reduced rehospitalizations, and greater satisfaction of the patient. In that regard, the analysis of the family nurse role in the municipality of Veles is important for understanding the needs of patients, professional tasks of nurses, and the possibilities for improving nursing care in the community (3).

AIM

The aim of the paper was to identify and analyze the work tasks of a family nurse in the care, treatment and education of postoperative patients in the municipality of Veles, with an emphasis on the importance of continuing health care after discharge from hospital. Based on the set goal, an attempt was made to examine the degree of involvement of family nurses in home postoperative care, the type of interventions they perform, the method of communication with patients and families, as well as the importance of health education in preventing complications and improving treatment outcomes.

Specific objectives of the work:

- To describe the most common nursing activities for postoperative patients at home;

- To determine how well are the patients informed are about proper surgical wound care, therapy, and possible complication signs;
 - To assess the level of patients' satisfaction with postoperative care received;
 - To analyze the experiences and challenges of family nurses in their work with postoperative patients;
- To point out the importance of education as part of professional nursing care.

It was expected that the work would contribute to a clearer definition of the family nurse's role in postoperative care and highlight the need for a systematic approach to monitoring, treating, and educating patients in the home setting.

MATERIALS AND METHODS

This was a quantitative, descriptive and cross-sectional study. This methodological approach was suitable for obtaining data on current conditions, experiences, attitudes and needs related to postoperative home care. The descriptive nature of the research enabled a systematic description of the role and work tasks of a family nurse, while the quantitative approach enabled the processing and comparison of the obtained data.

The research was conducted in the territory of the municipality of Veles. The study included two groups of respondents: postoperative patients and family nurses. The first group consisted of 30 postoperative patients discharged for home treatment after surgery who required monitoring, care, treatment or education. The second group consisted of 10 family nurses who were in contact with patients in the postoperative period (4).

Inclusion criteria: adults, patients in the postoperative period, patients being treated or recovering at home, and persons who voluntarily agreed to participate in the study.

Criteria for inclusion of family nurses: active professional work in primary or home health care and experience in work with postoperative patients.

The participation of all respondents was voluntary and anonymous.

A structured survey questionnaire was used as an instrument for data collection. The patients' questionnaire contained questions on basic sociodemographic data, type of postoperative care, frequency of home visits, information on wound care, therapy, nutrition, physical activity, symptom recognition, and level of satisfaction with the healthcare service provided. The questionnaire intended for family nurses included questions about their work tasks, how they assess patients, the interventions they most often perform, educational activities, communication with patients, and professional challenges (5).

The data collection procedure was carried out after previously informing the respondents about the purpose of the research. Respondents were informed that the data would be used exclusively for scientific research purposes, that personal data would not be published, and that they could withdraw from participation at any time. Thus, compliance with the basic ethical principles was ensured: voluntariness, anonymity, confidentiality and protection of the respondents' dignity (6).

The tasks of a family nurse were analyzed in several areas including: health assessment, surgical wound care, vital parameters monitoring, pain control, application and supervision of therapy, risk recognition, counseling on nutrition and physical activity, patient and family education, documentation management, and cooperation with the primary care physician. Accordingly, more complete picture of the practical role of the nurse in the postoperative period was obtained (7).

The collected data were processed using descriptive statistics. The results were presented through numbers, percentages, and comparative analysis between patients' and family nurses' responses. The interpretation was focused on whether the data obtained confirmed the importance of regular home care and health education in reducing the risk of complications and improving the quality of recovery.

Possible limitations of the study included the relatively small sample, the subjectivity of the responses, and the dependence of the data on the experience and memory of the respondents. However, this approach was appropriate for gaining initial insights into the state of practice and for identifying areas where postoperative patient care could be improved (8).

RESULTS

Table 1 **Sex of the Respondents.**

Sex	Number	%
Male	28	46.7
Female	32	53.3

Table 2 **Age of the Respondents.**

Age	Number	%
18–40	14	23.3
41–60	25	41.7
Over 60	21	35.0

Table 3 **Type of Surgery.**

Type	Number	%
Abdominal	20	33.3
Orthopedic	18	30.0
Gynecological	12	20.0
Other	10	16.7

Table 4 **Did the Family nurse visit the patient at home?**

Answer	Number	%
Yes	49	81.7
No	11	18.3

Table 5 **The most common tasks of a nurse.**

Task	% of patients
Monitoring vital parameters	88%
Wound dressing	76%
Providing therapy	71%
Nutrition education	69%
Hygiene tips	83%
Family support	61%

Table 6 **Satisfaction with the work of the nurse.**

Answer	Number	%
Excellent	31	51.7
Very good	19	31.7
Good	8	13.3
Dissatisfied	2	3.3

Table 7 **Did education help faster recovery?**

Answer	Number	%
Yes	52	86.7
No	8	13.3

DISCUSSION

The family nurse plays a significant role in home postoperative care.

- The most common activities are dressing, therapy, and monitoring.
- Patient's education significantly contributes the proces of recovery.
- Patients in Veles showed high satisfaction with the services.

Postoperative care is a complex process that requires organized monitoring, timely intervention and continuous education of the patient. In this process, the family nurse has an important professional role, as she provides health support during the period when the patient returns to the home environment and still requires professional assistance.

The tasks of a family nurse include several interrelated activities: health assessment, surgical wound care and control, vital signs monitoring, pain assessment, therapy administration, prevention and early recognition of complications, counseling, documentation and cooperation with the physician. These activities have preventive, therapeutic and educational importance (9).

Education of the patient and his family is one of the most important segments of postoperative care. Through clear and comprehensible instructions on hygiene, nutrition, movement, taking therapy and recognizing warning symptoms, the patient's independence increases thus reducing the possibility of inappropriate behavior at home (10).

It is important that the family nurse be recognized as an active provider of primary health care and as an important participant in postoperative treatment. Improving medical care, regular professional education, better organization of home visits and strengthened communication between healthcare professionals can contribute to better quality, safer and more humane care of postoperative patients in the municipality of Veles.

The results of the conducted research indicate the significant role of the family nurse in the process of postoperative care, treatment and education among patients in the municipality of Veles. The data obtained show that the majority of respondents were women (53.3%), while male patients participated with 46.7%. This difference is small, but may indicate a higher prevalence of surgical interventions in the female population, especially gynecological surgical procedures (11).

With regard to age, the highest percentage of patients was between 41 and 60 years old (41.7%), which was expected given that chronic diseases and conditions requiring surgical treatment were more common in this age group. There was also a significant number of patients over 60 (35%), whose recovery after surgery was slower and required more intensive medical care. The most common surgical procedures were abdominal surgeries (33.3%) and orthopedic interventions (30%). Those patients had

an increased need for wound control, pain, mobility, and monitoring for possible complications. This additionally emphasizes the need for regular home visits and the active involvement of the family nurse.

A particularly significant data was that 81.7% of patients were visited at home by a family nurse.

This data shows the good organization of primary health care in Veles and the availability of outpatient nursing services. Home visits enable timely detection of complications, monitoring of health status, and psychological support for the patient and family (12)

Analysis of work tasks shows that the most common activities were monitoring vital signs (88%), advising on personal hygiene (83%), dressing surgical wounds (76%), and providing therapy (71%). These results are in line with modern standards of nursing practice, according to which the nurse has a central role in monitoring the patient, preventing infections and improving general condition.

Nutrition and lifestyle education was provided to 69% of patients, which is very important given that proper nutrition and an appropriate lifestyle directly affect the healing process.

In addition, 61% of patients received support and counseling from their family, which shows that the nurse does not only work with the patient, but also with the patient's immediate environment.

Satisfaction with the work of the family nurse was high, with 51.7% of patients rating the service as excellent and 31.7% as very good. This result indicates trust in medical staff and a positive perception of service quality. Only a small number of respondents were dissatisfied (3.3%), which might be a consequence of individual expectations, insufficient visit frequency or organizational reasons.

Especially important is the fact that 86.7% of patients believed that the education received from the nurse contributed to faster recovery. This confirms that the educational role of the nurse is as important as practical care. An informed patient can more easily follow the therapy, take proper care of

the wound and recognize warning symptoms in a timely manner.

In summary, the results show that the family nurse plays a key role in the postoperative period through care, monitoring, treatment and health education. Her presence contributes to reducing complications, faster recovery and a better quality of life for patients in the municipality of Veles.

Study limitations

The research was conducted on a relatively small sample of 60 respondents and in one municipality, thus the results cannot be fully generalized to the entire country. Future research with a larger number of respondents and comparisons between different regions is recommended.

Recommendations:

- Increasing the number of home visits for patients at risk.
- Continuous education of medical staff.
- Improving coordination between surgeons, family doctors and nurses.
- Development of a home postoperative care program in the local community.

CONCLUSION

Postoperative care is a complex process that requires organized monitoring, timely intervention and continuous education of the patient. In this process, the family nurse has an important professional role, as she provides health support during the period when the patient returns to the home environment and still require professional assistance. Based on the results obtained, it can be concluded that the family nurse has a significant and irreplaceable role in the postoperative care of patients in the Municipality of Veles. It is important that the family nurse be recognized as an active provider of primary health care and an important participant in postoperative treatment. Improving medical care, regular professional education, better organization of home visits and strengthened communication between healthcare professionals can contribute to better quality, safer and more

humane care of postoperative patients in the municipality of Veles.

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Authors' Contributions: BN, GP and GK-M contributed significantly to the conception and design of the article, as well as the acquisition, analysis, and interpretation of data for the work. Each author had a role in drafting of the article and the revision process. Each author gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial support and sponsorship: nil.

Conflict of interest: there are no conflicts of interest.

The Key Role of The Midwife in Support, Preparation and Assistance During Instrumental Vaginal Births, With a Special Emphasis on the Care of the Mother and Baby After Delivery

Ključna uloga babice u podršci, pripremi i asistenciji tokom instrumentalnih vaginalnih porođaja, s posebnim naglaskom na njegu majke i bebe nakon porođaja

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ABSTRACT

Introduction: Instrumental vaginal delivery represents an important obstetric intervention used in situations where it is necessary to expedite delivery or prevent risks to the mother and the fetus. In such cases, the role of the midwife is essential, as she provides continuous care, support, and professional assistance throughout all stages of childbirth.

Aim: to analyze the key role of the midwife in the preparation, support, and assistance during instrumental vaginal deliveries, with special emphasis on postpartum care for both the mother and the newborn.

Materials and methods: The study included a total of 30 midwives who participated in a survey consisting of 10 questions.

Results: The paper examined the theoretical aspects of instrumental deliveries, including indications and possible complications, as well as the specific responsibilities and activities of the midwife. Special attention is given to the postpartum period,

during which the midwife plays a crucial role in monitoring the mother's condition, preventing complications, and ensuring appropriate care for the newborn, including breastfeeding support and the establishment of early mother-infant bonding.

Conclusion: The findings indicate that the midwife is an indispensable part of the healthcare team, whose expertise and care directly influence the outcome of delivery and the well-being of both the mother and the newborn.

Keywords: midwife, instrumental delivery, vacuum extraction, forceps, postpartum care, newborn

SAŽETAK

Uvod: Instrumentalni vaginalni porođaj je značajna akušerska intervencija koja se koristi u slučajevima kada je potrebno ubrzati porođaj ili spriječiti rizike za majku i fetus. U tim situacijama, uloga babice je neophodna, jer ona pruža kontinuiranu njegu, podršku i stručnu pomoć tokom svih faza porođaja.

Cilj: analizirati ključnu ulogu babice u pripremi, podršci i asistenciji tokom instrumentalnih vaginalnih porođaja, sa posebnim fokusom na postporođajnu negu majke i novorođenčeta.

Materijali i metode: Studija je obuhvatila ukupno 30 babica koje su učestvovala u anketi koja se sastojala od 10 pitanja.

Rezultati: Rad razmatra teorijske aspekte instrumentalnih porođaja, indikacije i moguće komplikacije, kao i specifične aktivnosti i odgovornosti babice. Posebna pažnja posvećena je postporođajnom periodu, gdje babica ima ključnu ulogu u praćenju stanja majke, sprječavanju komplikacija i pružanju odgovarajuće njege novorođenčetu, uključujući podršku dojenju i uspostavljanje rane veze majka-beba.

Zaključak: Analize ukazuju na to da je babica neizostavan dio zdravstvenog tima, čija stručnost i briga direktno utiču na ishod porođaja i dobrobit majke i novorođenčeta.

Ključne riječi: babica, instrumentalni porođaj, vakuum ekstrakcija, forceps, postporođajna njega, novorođenče

INTRODUCTION

Childbirth is a natural physiological process, but in certain situations it can be complicated and require medical intervention to preserve the health and life of the mother and newborn. Instrumental vaginal delivery, involving the use of forceps or vacuum extractors, is an important obstetric procedure used in cases where spontaneous labor is not progressing adequately or when there is a risk of fetal distress. Although these interventions are of great importance in modern obstetric practice, they also require a high level of expertise, coordination, and a careful approach of the healthcare team (1).

In that regard, the midwife has a central and multidimensional role. She is not just a passive assistant in the process, but an active participant who provides continuous care, support, and monitoring of the mother and fetus. The role of the

midwife begins during pregnancy, continues during childbirth, and is especially manifested in situations where instrumental intervention is required. Before the very instrumental birth, the midwife has the task of preparing the postpartum woman both physically and psychologically, by providing appropriate information, reducing fear and anxiety, as well as creating a sense of security and trust.

During the intervention itself, she actively participates in offering assistance, ensures sterile conditions, monitors the course of labor and vital parameters of the mother and fetus, and provides continuous support (2). The role of the midwife is especially important in the postpartum period, which is a sensitive phase for both the mother and newborn. During this period, the midwife is responsible for early recognition of possible complications, such as postpartum hemorrhage, infections, or breastfeeding problems. In addition, it plays a key role in establishing the first contact between mother and baby, encouraging breastfeeding, and providing appropriate care for the newborn. Modern health standards emphasize the need for a holistic approach to maternal care, where not only physical, but also psychological and emotional aspects are taken into account. In that regard, the midwife is a key link in providing quality, safe and humane care.

Instrumental vaginal births are obstetric interventions in which the birth is completed vaginally with the help of special instruments, most often forceps or a vacuum extractor (3). This procedure is used when spontaneous labor is not progressing adequately or when there is a risk to the health of the mother and/or fetus, and vaginal delivery is still possible and safe. The goal of instrumental births is to shorten the duration of the second stage of labor and prevent complications, while avoiding cesarean section when justified (4).

Although instrumental delivery is performed by an obstetrician-gynecologist, the midwife plays an important role in the entire process. She participates in the preparation, provides assistance during the intervention, and plays a key role in monitoring the condition of the mother and newborn after delivery.

The role of the midwife before delivery is a key segment in ensuring a safe and successful outcome of childbirth, especially when there is a possibility of instrumental intervention. This period includes the physical, psychological and educational preparation of the mother, and continuous monitoring of her condition and the condition of the fetus (5).

A midwife is a healthcare professional who has direct contact with a pregnant woman and plays a significant role in creating trust, reducing fear, and ensuring safety throughout the entire process.

Psychological support is of utmost importance, especially when there is a possibility of instrumental delivery, which often causes fear and anxiety in the new mother (6).

AIM

The aim of this paper was to analyze and present the key role of the midwife in support, preparation and assistance during instrumental vaginal births, with special emphasis on postpartum care of the mother and newborn. Through theoretical analysis and, where applicable, practical research emphasized the importance of the midwife as a provider of care and safety at one of the most important moments in a woman's life.

MATERIALS AND METHODS

The study was conducted through a survey consisting of 10 questions, intended for midwives working in gynecological and obstetric departments. The study included a total of 100 midwives.

RESULTS

Table 1 Do you participate in preparing the new mother for instrumental delivery?

Answer	No.	%
Yes	93	93%
NO	7	7%

Table 2 Do you provide psychological support?

Answer	No.	%
Yes	100	100%
No	0	0%

Table 3 Do you assist with instrumental births?

Answer	No.	%
Yes	90	90%
No	10	10%

Table 4 Do you perform fetal monitoring (CTG)?

Answer	No.	%
Yes	97	97%
No	3	3%

Table 5 Are you involved in the mother's postpartum care?

Answer	No.	%
Yes	100	100%
No	0	0%

Table 6 Do you support breastfeeding?

Answer	No.	%
Yes	93	93%
No	7	7%

Table 7 Do you think that the midwife plays a key role in instrumental births?

Answer	No.	%
Yes	100	100%
No	0	0%

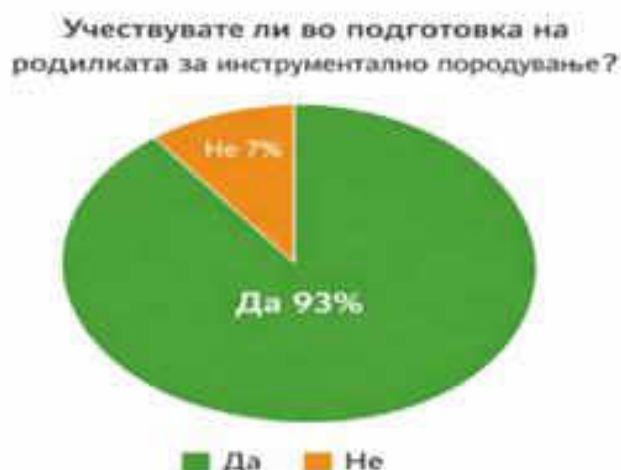


Figure 1 How many midwives actively participated in preparation of a new mother before instrumental birth?

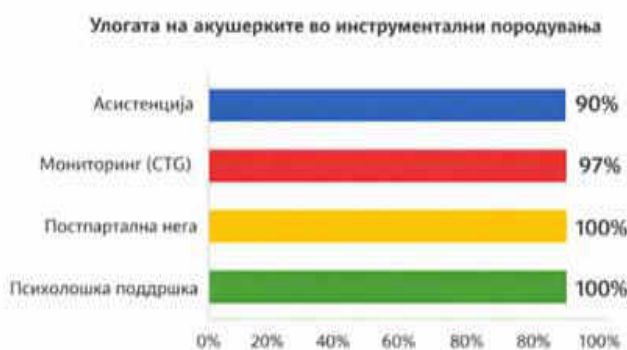


Figure 2 Direct midwife assistance during instrumental delivery.

Figure 1 shows that majority of midwives (93%) took active participation, whereas only a small number (7%) did not participate.

Figure 2 shows that 90% of midwives had significant majority role whereas only a small number (10%) was not included.

DISCUSSION

The results obtained clearly indicate that the midwife has a central role in all phases of instrumental delivery. Her role in psychological support, monitoring and postpartum care is

particularly emphasized. The results are consistent with modern obstetric practices, which recognize the midwife as a key part of the healthcare team. The study confirms that the midwife plays an irreplaceable role in: preparing the mother for labor, assisting during the intervention, and providing postpartum care. Her expertise, care, and support directly impact the health and safety of the mother and newborn. The survey shows that 93% of mothers received preparation, only 7% of them did not get any advice. The site had psychological support (0% of mothers had good assistance during instrumental delivery. 97% of them confirmed that they had fetal monitoring (CTG). 100% of midwives were involved in postpartum care of the mother. 93% of mothers got support in breastfeeding. Midwives are 100% the greatest support for every mother (7). Figure 1 shows that the majority of midwives (93%) had active participation, whereas only a small number (7%) did not participate. Figure 2 shows that 90% of midwives had a significant majority role, whereas only a small number (10%) was not included.

CONCLUSION

Based on theoretical analysis and the study results, it can be concluded that the midwife plays a key and irreplaceable role in instrumental vaginal deliveries. Her role begins in the prenatal period, where she provides psychological and physical preparation for the mother, contributing to reducing fear and improving cooperation. During instrumental delivery, the midwife actively participates in ensures sterile conditions, performs continuous monitoring of the mother and fetus, and provides emotional support. Her role is especially important in the postpartum period, where she provides comprehensive care to the mother and newborn. Research results further confirm this role, showing that midwives actively participate in all stages of childbirth and have a significant impact on the outcome.

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Authors' contributions: TP, GK-M and, GP gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial support and sponsorship: nil.

Conflict of interest: there are no conflicts of interest.

The Role of the Visiting Nurse in the Prevention and Early Detection of Diseases in Young Children

Uloga patronažne sestre u prevenciji i ranom otkrivanju bolesti kod male djece

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ABSTRACT

Introduction: Visiting nurse has a key role in primary health care, especially in the prevention and early detection of diseases in young children.

Ai: to examine the importance and impact of visiting nurses on the health and development of children through preventive activities, health education and early recognition of diseases.

Materials and methods: The paper analyzes the basic tasks of community nurses, including home visits, monitoring the growth and development of children, advising parents on proper nutrition, hygiene and immunization, as well as early recognition of health and developmental problems. Special emphasis was placed on the role of the monitoring service in the education of parents and its impact on reducing morbidity in the child population.

Results: indicate that the continuous work of visiting nurses significantly contributes to the improvement of the health condition of children, the timely detection of diseases and the prevention of complications. Parental education has proven to be an important factor in creating healthy habits and improving children's health.

Conclusion: the public health care nurse is an indispensable part of the health system, with an important role in preventive medicine and the protection of children's health.

Keywords: public health nurse, prevention, early detection, children, health education

SAŽETAK

Uvod: Patronažna sestra ima ključnu ulogu u primarnoj zdravstvenoj zaštiti, posebno u prevenciji i ranom otkrivanju bolesti kod male djece.

Cilj: ispitati značaj i utjecaj patronažne sestre na zdravlje i razvoj djece kroz preventivne aktivnosti, zdravstveno obrazovanje i rano prepoznavanje bolesti.

Materijali i metode: Rad analizira osnovne zadatke patronažne sestre, uključujući kućne posjete, praćenje rasta i razvoja djeteta, savjetovanje roditelja o pravilnoj ishrani, higijeni i imunizaciji, kao i rano prepoznavanje zdravstvenih i razvojnih problema. Poseban naglasak stavljen je na ulogu patronažne službe u edukaciji roditelja i njen utjecaj na smanjenje morbiditeta u dječjoj populaciji.

Rezultati: Ukazuju da kontinuirani rad patронаžne sestre značajno doprinosi poboljšanju zdravstvenog stanja djece, pravovremenom otkrivanju bolesti i prevenciji komplikacija. Edukacija roditelja se pokazuje kao važan faktor u stvaranju zdravih navika i poboljšanju zdravlja djece.

Zaključak: Medicinska sestra javnog zdravstva neizostavan dio zdravstvenog sistema, sa značajnom ulogom u preventivnoj medicini i zaštiti zdravlja djece.

Ključne riječi: medicinska sestra javnog zdravstva, prevencija, rano otkrivanje, djeca, zdravstveno obrazovanje

INTRODUCTION

Children's health from an early age is the basis for proper growth, development and quality of life in the future. Early childhood is a sensitive period in which children are especially susceptible to various diseases, developmental disorders and risks that can have long-term consequences. Therefore, prevention and early detection of disease are key factors in modern healthcare.

The visiting nurse plays an important role in primary health care, especially in working with newborns, infants and young children. Her work takes place in a home environment, which allows for direct insight into the child's environment, family conditions, and habits. This approach enables timely recognition of potential risks to the child's health and development (1).

One of the main tasks of the visiting nurse is the health education of parents. She advises them on proper nutrition, breastfeeding, vaccinations, hygiene, and how to recognize early illness symptoms. Through continuous communication and counseling, the visiting nurse contributes to improving health habits and reducing risk factors. Early detection of the disease is particularly important as it allows for timely intervention and prevention of complications (2). The visiting nurse plays a key role in monitoring the child's growth and development, identifying deviations and referring

them to appropriate health facilities. She actively participates in screening programs and monitoring the immunization status of children. In addition, the visiting nurse plays an important role in the early detection of social and psychological family problems that can affect the child's health. Through an individual approach and a confidential relationship with the family, she contributes to the creation of a safe and supportive environment for the child. Modern healthcare systems increasingly recognize the role of community health services as a key element in preventive medicine. Investing in this service contributes to reducing morbidity and mortality in children, as well as improving the general health of the population (3).

Home health care service and its importance

The home health care service is an integral part of primary health care and has a significant role in improving the health of the population, especially among vulnerable categories such as newborns, infants and small children. This service is based on the preventive medicine principles, continuous care, and an individual approach to the patient and his/her family. A home health nurse performs her work in a home environment, which enables her to have direct insight into the living environment, social conditions, and health habits of the family. This approach is of particular importance given that many factors affecting a child's health derive from the home environment. In addition to medical activities, home health care services also have a social and educational role. The services also contribute to improving the health culture of the population and reducing health inequalities (4).

The role and tasks of the home health care nurse

The home health nurse has a wide range of tasks aimed at preserving and improving the child's health. Her work includes the following:

Home visits

Home visits are a fundamental segment of a visiting nurse's work. They enable: assessing the child's health status, monitoring growth and

development, assessing hygienic and social conditions, and establishing trust with the family.

Monitoring growth and development

Regular monitoring of physical and psychomotor development is essential for early detection of deviations. The following is monitored: body weight and height, motor development, cognitive and speech development and social behavior

Health education

The visiting nurse plays an important role in educating parents about: breastfeeding and proper nutrition, hygiene and child care, vaccinations, and recognizing symptoms of illness.

Early disease detection

Through regular visits and observation, the nurse can timely identify: infections, developmental disorders, nutritional deficiencies and chronic diseases.

Referral and cooperation

In case of suspected health problems, the visiting nurse refers the child to the appropriate doctor and cooperates with: pediatricians, family doctors and social services.

Disease prevention in children

Prevention is a key aspect in children's health care and can be divided into:

Primarna prevencija - It refers to preventing the occurrence of diseases through: immunization, proper nutrition, maintenance of hygienic and healthy lifestyle habits. The public health nurse has an important role in promoting these measures.

Secondary prevention - It refers to early detection of disease and timely treatment and includes: screening, regular check-ups, and early recognition of symptoms.

Tertiary prevention - The aim is to prevent complications and disability in already ill children

through: rehabilitation, ongoing care, and family support.

Early detection of disease

Early detection is essential for successful treatment and a better outcome. It enables: timely therapy initiation, prevention of complications and a better quality of life. The visiting nurse plays a key role through: observing symptoms, monitoring developmental parameters, and communicating with parents. The most common early detected conditions include: respiratory infections, anemia, eating disorders, and developmental delays (5).

Health education of parents

Parental education is the basis of prevention. An informed parent can: recognize symptoms in a timely manner, react appropriately, and ensure a healthy environment. The home health nurse uses various methods such as: individual counseling, demonstrations, and educational materials. Topics most frequently covered include: breastfeeding, introducing complementary foods, hygiene, vaccinations and child safety (6).

The most common diseases in young children

Young children are susceptible to various diseases, such as: respiratory infections (colds, bronchitis and pneumonia), gastrointestinal diseases (diarrhea, vomiting and dehydration), nutritional disorders (anemia, malnutrition and obesity), developmental disorders (speech delay, motor problems and cognitive disorders) (7,8).

Social factors and their influence

A child's health depends not only on medical factors, but also on: economic status, parents' education, living conditions and family support. The visiting nurse identifies these factors and suggests measures to overcome them (9).

The importance of community care in the modern healthcare system

In the modern healthcare system, the emphasis is on prevention. Home health care: reduces the burden on hospitals, enables early intervention and improves the health status of the population. Investing in this service is of great importance for the public health system. The visiting nurse plays an irreplaceable role in the prevention and early detection of diseases in children from a young age. Her work directly impacts the health, development and the child's quality of life. Through education, monitoring, and timely intervention, she is a key factor in modern healthcare.

AIM

The main objective of this paper was to examine the role of the visiting nurse in the prevention and early detection of diseases in young children, to analyze the tasks of the community nurse, determine the importance of health education of parents, examine the role in early detection of diseases, determine the impact of community care on children's health, and to propose measures to improve community care services.

Hypotheses

Home health nurses play a significant role in preventing illness in children.

- Early detection through home health care reduces the risk of complications
- Parental education contributes to better child health

MATERIALS AND METHODS

The research was conducted in the territory of Strumica in the period from January to March 2025. The research included 100 parents of children aged 0 to 5 who were visited by a community nurse.

Inclusion criteria: parents with children up to 5 years of age using patronage services.

Exclusion criteria: parents not visited by a community nurse and incomplete surveys.

Data was collected based on Survey-questionnaire, consists of 15 questions, divided into several parts: demographic data, experience with a community nurse, level of information, and early detection of the disease.

The survey included YES/NO and multiple choice questions, and 1-5 scale.

The data were processed using descriptive statistics, percentages, and tabular and graphical presentation.

RESULTS

Parents

Table 1 Demographic characteristics.

Characteristics	No. (n)	%
Women	78	78%
Men	22	22%
Age 20–30	40	40%
Age 31–40	45	45%
>40 years of age	15	15%

Table 2 Did a community nurse visit you?

Answer	No.	%
Yes	92	92%
No	8	8%

Table 3 How often were you visited?

Visits	No.	%
1–2 visits	20	20%
3–5 visits	50	50%
>5 visits	22	22%
No visits	8	8%

Table 4 Did you receive education from the visiting nurse?

Answer	No.	%
Yes	88	88%
No	12	12%

Table 5 Which topics were you educated on?

Topic	%
Breast-feeding	75%
Diet	82%
Hygiene	90%
Vaccination	85%

Table 6 Did the community nurse help in early detection of problems?

Answer	No.	%
Yes	60	60%
No	40	40%

Table 7 Which problems were detected?

Problem	%
Anemia	20%
Infection	30%
Developmental delays	25%
Nutritional problems	25%

Table 8 Satisfaction rate (1-5).

Rate	%
1	2%
2	3%
3	15%
4	40%
5	40%

Table 9 Does a community nurse contribute to better child health?

Answer	%
Yes	85%
No	15%

Nurses

Table 1 Demographic characteristics.

Characteristic	No.	%
Women	78	78%
Men	22	22%
20–30 yeras	40	40%
31–40 years	45	45%
>40 years of age	15	15%

Table 2 Visits by a community nurse.

Answer	No.	%
Yes	92	92%
No	8	8%

Table 3 Frequency of visits.

Visits	No.	%
1–2 visits	20	20%
3–5 visits	50	50%
>5 visits	22	22%
No visits	8	8%

Table 4 Health education.

Answer	No.	%
Yes	88	88%
No	12	12%

Table 5 Early detection.

Answer	No.	%
Yes	60	60%
No	40	40%

Table 6 Satisfaction.

Rate	%
1	2%
2	3%
3	15%
4	40%
5	40%

DISCUSSION

The results of this study confirm the important role of home care nurses in the prevention and early detection of illness in young children. The findings are in line with contemporary scientific knowledge and recommendations from relevant international health organizations such as the World Health Organization and UNICEF, which emphasize the importance of primary health care and home visits as key mechanisms for promoting child health.

Regarding coverage of home health visits, the results showed that 92% of respondents were visited by a home health nurse. This high percentage is in line with research from the World Health Organization, which highlights that regular home visits significantly reduce the risk of illness in children and improve parents' health education. However, the remaining percentage of 8% indicates that there are still some gaps in coverage, which presents a challenge for the health system. The results of the study show that 88% of parents received health education from a home care nurse. This is in line with UNICEF studies, which indicate that parent education is one of the most effective ways to prevent illness in children.

It is particularly significant that most of the education relates to hygiene, nutrition, and vaccination, which are considered key factors in reducing morbidity in the child population. Regarding early detection, 60% of respondents stated that the community nurse helped in the timely detection of certain health problems. This result is consistent with research published by the Centers for Disease Control and Prevention, which highlights that early detection of health conditions significantly improves treatment outcomes and reduces the risk of complications.

The analysis of the types of problems detected (infections, anemia, developmental delays and eating disorders) is consistent with global data, according to which these conditions are most common in young children. According to the World Health Organization, these diseases are the leading causes of morbidity in children, which further

emphasizes the importance of community health services.

Parents' satisfaction with the services of the community nurse is also an important indicator. In this study, 80% of respondents gave a high score (4 and 5), which indicates a positive perception of service quality. This finding is consistent with studies showing that trust and communication between the health care provider and the family are crucial for successful health intervention.

In addition, 85% of respondents believe that the community nurse has a direct impact on improving the child's health. This confirms the importance of preventive activities and continuous care, which is in line with the concept of primary health care promoted by the World Health Organization.

However, the study also has certain limitations. The sample is relatively small (100 respondents) and geographically limited to one municipality, which may affect the generalization of the results. Also, the data is based on parents' self-assessment, which can result in subjectivity.

Future studies should have a larger sample, inclusion of more regions, and a combination of quantitative and qualitative methods. The discussion shows that the research results are in line with global trends and scientific literature. The community nurse is a key factor in the prevention and early detection of diseases in children, and her role should be further strengthened and improved within the healthcare system.

CONCLUSION

The home care nurse is one of the most important pillars of primary health care, especially in the area of health care for children from an early age. Through her continuous and comprehensive work in home conditions, the community nurse ensures timely prevention, early detection of diseases and appropriate health education for parents. Parental education has proven to be a key factor in disease prevention. Informed parents have a greater ability to recognize early symptoms, apply

proper health practices, and create a safe and healthy environment for their children. In this context, the community nurse has not only a medical role, but also a significant pedagogical and advisory role. Despite the positive results, the research also points to the need for further improvement of the community care service. It is necessary to increase the volume, continuously educate health staff and improve coordination with other health and social institutions.

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Authors' contributions: SI, GP, GK-M and MB gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial support and sponsorship: nil.

Conflict of interest: there are no conflicts of interest

The Role of the Nurse in Understanding the Parents' Experiences of Children with Type 1 Diabetes Mellitus

Uloga medicinske sestre u razumijevanju iskustava roditelja djece s dijabetes melitusom tipa 1

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ABSTRACT

Introduction: Diabetes mellitus type 1 is one of the most common chronic diseases of childhood requiring continuous care, daily glycemic control, the use of insulin therapy and significant involvement of parents in the treatment process. The diagnosis of the disease in a child often causes emotional stress, fear, insecurity and changes in everyday life. The nurse has an important role in education, psychological support and understanding the experience of parents during the process of adaptation to the disease.

Aim: to present the role of nurses in understanding the experiences of parents of children with type 1 diabetes mellitus, with special emphasis on education, emotional support and improving the family's quality of life.

Materials and methods: The work was designed as a review of the available professional and scientific literature in the field of pediatric endocrinology, nursing and health education. Relevant professional journals, guidelines and publications related to the experiences of parents of children with type 1 diabetes mellitus and the role of nurses in the health care process were used.

Results: The analysis of the literature shows that parents of children with type 1 diabetes mellitus go through various emotional and organizational challenges after diagnosis. Continuous education, availability of nurses, developed communication and an individualized approach contribute to a better understanding of the disease, a greater sense of security for parents and more successful disease control in children. Nurses represent an important link between children, families and the multidisciplinary team, and actively participate in empowering parents for daily care of the child.

Conclusion: The nurse's role in understanding the parents' experience of children with diabetes mellitus type 1 has a significant impact on the quality of health care and the process of family adaptation to chronic disease. Professional support, continuous education and an empathetic approach contribute to reducing fear and strengthening the competence of parents in the daily care of the child.

Keywords: diabetes mellitus type 1, nurse, education, parents' experience.

SAŽETAK

Uvod: Diabetes mellitus tip 1 predstavlja jedno od najčešćih hroničnih oboljenja dječije dobi koje zahtijevaju kontinuiranu brigu, svakodnevnu kontrolu glikemije, primjenu inzulinske terapije i značajnu uključenost roditelja u procesu liječenja. Dijagnoza bolesti kod djeteta često izaziva emocionalni stres, strah, nesigurnost i promjene u svakodnevnom životu. Medicinska sestra ima važnu ulogu u edukaciji, psihološkoj podršci i razumijevanju iskustva roditelja tokom procesa prilagodbe na bolest.

Cilj: prikazati ulogu medicinske sestre u razumijevanju iskustva roditelja djece sa diabetes mellitusom tip 1, sa posebnim osvrtom na edukaciju, emocionalnu podršku i unapređenje kvaliteta života porodice.

Materijali i metode: Rad je koncipiran kao pregledni stručni rad na analizi dostupne stručne i naučne literature iz oblasti pedijatrijske endokrinologije, sestinstva i zdravstvene edukacije. Korišteni su relevantni stručni časopisi, smjernice i publikacije koje se odnose na iskustva roditelja djece oboljele od diabetes mellitus tip1 i ulogu medicinske sestre u procesu zdravstvene njege.

Rezultati: Analiza literature pokazuje da roditelji djece sa diabetes mellitusom tip 1 prolaze kroz različite emocionalne i organizacijske izazove nakon postavljanja dijagnoze. Kontinuirana edukacija, dostupnost medicinske sestre, razvijena komunikacija i individualizirani pristup doprinose boljem razumijevanju bolesti, većem osjećaju sigurnosti roditelja i uspješnijoj kontroli bolesti kod djece. Medicinska sestra predstavlja važnu poveznicu između djece, porodice i multidisciplinarnog tima, te aktivno učestvuje u osnaživanju roditelja za svakodnevno zbrinjavanje djeteta.

Zaključak: uloga medicinske sestre u razumijevanju iskustva roditelja djece sa diabetes mellitusom tip 1 ima značajan uticaj na kvalitet zdravstvene njege i procesu prilagodbe porodice na hroničnu bolest. Profesionalna podrška, kontinuirana edukacija i empatijski pristup doprinose smanjenju straha i jačanju kompetencija roditelja u svakodnevnoj brizi za dijete.

Ključne riječi: diabetes mellitus tip 1, medicinska sestra, edukacija, iskustvo roditelja

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is caused by the progressive autoimmune destruction of insulin-producing pancreatic beta cells in genetically predisposed individuals (1,2,3). T1DM is one of the most common chronic pathologies in children (4), it is complex and invasive (5,6), and difficult to control as it involves various physical, clinical, and psychosocial complications for the affected individual (6). The incidence of T1DM is increasing worldwide (1,5,7,8,9) and it is the third most common chronic condition in childhood (10). In Bosnia and Herzegovina, the annual incidence of T1DM is 10-14 per 100,000 children (10). In 2006, the UN declared T1DM to be one of the major threats to global health (11), arguing that this increase is a reflection of modern lifestyles (9,12).

Unlike other pathologies where decisions about care are made exclusively by medical experts, many responsibilities for daily control and care rest with children, adolescents and their parents/guardians, very often immediately and after the diagnosis is established (12). This chronic disease requires an intensive effort by the child and its parents/guardians in following the recommendations in order to keep the disease under control (13). DMT1 has high treatment costs in the health care system, which increases with its frequency and lack of adherence and self-control (12). Comorbidities accompanying this disease are as harmful as the disease itself (14).

For many families, the diagnosis of DMT1 in their child creates significant trauma. This results in a state of shock, feelings of pain, anger, isolation due to the complex, invasive nature of the disease, and coping with a new lifestyle (6,12,15). In addition to changes in family habits and lifestyles, uncertainty about the child's future, thoughts about acute and chronic complications, various psychosocial problems arise in children, adolescents, their families and their immediate surroundings (2). The support parents/caregivers receive at the very diagnosis of

DMT1 in their child is of great importance for their self-confidence, as well as the child's self-confidence, leading to better adherence to treatment, better control of DMT1, better overall perception of quality of life and reduced complications (12).

ADA, according to "Standards for medical care in diabetes – 2016", recommends regular assessment of psychosocial aspects and quality of life, both of children with DMT1, adolescents, and their families, in order to avoid depression, anxiety, and problems with nutrition (12,16).

Education is an approach that is considered an integral and permanent part of patient care. Education helps patients acquire or maintain the skills they need for self-management and good regulation of DMT1. It includes organized activities designed to introduce the patient and their parents/caregivers to understand DMT1 and treatment, work together, take responsibility for self/child care, maintain and improve quality of life (17). The information they receive during education should serve as a basis for setting up a personalized program of therapeutic education (17).

DMT1 requires daily treatment and can have serious consequences on the quality of life of children and their parents/guardians, the entire family, and its current state and future health (17). Treatment should be started systematically by a team of experts (pediatrician, nurse-educator, dietician and psychologist), which is the key to successful management of DMT1 and has a favorable result on glycemic control and psychosocial outcomes (17).

Education of parents/caregivers plays an important role not only in improving the quality of life of a sick child, but also in preventing or delaying later complications of the disease (18).

Health education is a key resource in helping patients understand and engage in the management of their health condition (19).

AIM

The aim of this paper was to present the role of the nurse in understanding the parents' experiences of children with type 1 diabetes, with a special focus on education, emotional support and improving the quality of life of the family.

MATERIALS AND METHODS

The paper was designed as a review of the available professional and scientific literature in the field of pediatric endocrinology, nursing and health education. Relevant professional journals, guidelines and publications related to the experiences of parents of children with type 1 diabetes mellitus and the role of the nurse in the health care process were used.

RESULTS

Haegele JA., et al. (20)	Understanding experiences of children with type 1 diabetes
Tong HJ., et al. (21)	Parents' experience of caring for children with type 1 diabetes in mainland China
Macaulay GC., et al. (22)	Sleep and night-time caregiving in parents of children and adolescents with type 1 diabetes mellitus
Holmstrom HR., et al. (23)	Parents' experiences of children with diabetes type 1
Xiros E., et al. (24)	The quality of life of parents of children with diabetes type 1
Souza RR., et al. (25)	Caring for diabetes at home

DISCUSSION

Parenting is often described as a stressful experience, which can be further complicated or made more stressful by causing anxiety when

parenting children with chronic illnesses such as T1DM. The incidence of DMT1 among children has increased and continues to increase globally, resulting in a need to understand the parents' experiences of children with DMT1. Parents are very often financially burdened; they have a fear of expanding the family, a fear of ups and downs with negative social interactions with other parents, with serious social and psychological consequences for the entire family (Haegle JA, et al.) (20).

The role of the nurse in understanding the parents' experience of children with diabetes mellitus type 1 has a significant impact on the quality of health care and the process of family adaptation to chronic disease. Professional support, continuous education and an empathetic approach contribute to reducing fear and strengthening the competence of parents in the daily care of the child (Tong HJ, et al.) (21).

Parents often have a fear of night care, possible hypoglycemia, which results in sleep disturbance (Macaulay GC, et al.) (22).

Frequently, the burden on parents and insufficient sleep has an impact on the quality of life of the entire family (Holmstrom, et al.) (23).

In this regard, social support plays an important role in reducing their fear and feelings of isolation from society (Xiros E, et al.) (24).

Providing social support at all levels of health care and giving adequate guidelines to parents would reduce concerns about eating habits, metabolic control and the use of therapy (Souza RR, et al.) (25).

CONCLUSION

DMT1 is a common chronic disease in children. Parents of children with DMT1 are under a lot of stress and constant worry. The experience of parental caregivers may influence the health outcomes of children with T1DM. Since self-care of children with DMT1 is a tiring and demanding caregiving task, it is extremely challenging for parents and their children, who are at an important

stage of physical and psychological development. Parents of children with DMT1 often feel isolated and helpless when faced with the complex and lengthy treatment of the disease. They have numerous needs in the process of adjusting to the diagnosis and care for DMT1. Parents of pediatric patients are troubled by various problems in the treatment of children's diseases, and this feeling persists during the complex daily management process. Parents constantly worry about their children's hypoglycemia and various DMT1 emergencies. Under the specific background of family, education, medical care, it is necessary to discuss in detail the experiences of parents and in different stages of the disease in order to help and support parents in adapting to the parental role of caregivers. Nurses should provide professional guidance in terms of information, skills, emotions and social support to parents. DMT1 care teams should be aware of DM-related factors that potentially affect parental sleep, the confounding effects of diabetes technologies, and consider tailored parental support and education to reduce the burden of nocturnal worries. The nurse's role in understanding the experience of parents of children with T1DM has a significant impact on the quality of health care and the process of family adaptation to chronic illness. Professional support, continuous education and an empathetic approach contribute to reducing fear and strengthening the competence of parents in the daily care of the child.

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Authors' Contributions: EH, AH, EM and EK contributed significantly to the conception and design of the article, as well as the acquisition, analysis, and interpretation of data for the work. Each author had a role in drafting of the article and the revision process. Each author gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial Support and Sponsorship: nil.

Conflict of Interest: there are no conflicts of interest.

Nurse-Led Transitional Care Interventions and Patient Outcomes: A Systematic Review 2020–2025

Intervencije tranzicijske skrbi vođene medicinskim sestrama i ishodi liječenja pacijenata: sustavni pregled literature (2020.–2025.)

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ABSTRACT

Introduction: Transitional care refers to coordinated, time-limited services that support continuity of care during patient transfers between healthcare settings. Nurse-led interventions such as discharge planning, patient education, medication reconciliation, and post-discharge follow-up aim to prevent gaps in care and reduce readmissions.

Aim: This review synthesised recent evidence on the effectiveness of nurse-led transitional care for adult patients, focusing on hospital readmissions, emergency department visits, mortality, quality of life, and patient satisfaction.

Materials and methods: A systematic PubMed search (January 2020 to September 2025) identified randomized and controlled studies, observational evaluations, protocols with defined outcomes, and systematic reviews or meta-analyses in English or Croatian. Predefined inclusion and exclusion criteria were applied. Thirty-one records were screened, and seventeen studies met the eligibility criteria.

Results: The studies showed that nurse-led transitional care often reduces unplanned readmissions, enhances continuity of care, and improves quality of life and satisfaction, particularly among older adults, patients with heart failure, and those after sepsis or stroke. Telehealth-supported models were generally feasible and acceptable. However, effects on mortality and emergency department use were inconsistent, and one economic evaluation reported that a complex transitional programme was not cost-effective.

Conclusion: Current evidence indicates that nurse-led transitional care can improve post-discharge outcomes and patient experience, although effectiveness depends on patient risk profile, intervention components, and organisational context. For health systems such as Croatia's, structured nurse-led transitional programmes may help reduce readmissions and support more efficient use of resources, but further pragmatic and economic studies are needed.

Keywords: transitional care, nurse-led interventions, hospital discharge, continuity of care, readmissions, patient outcomes

SAŽETAK

Uvod: Tranzicijska skrb odnosi se na koordinirane, vremenski ograničene usluge koje osiguravaju kontinuitet zdravstvene skrbi tijekom premještanja bolesnika između različitih razina i ustanova zdravstvenog sustava. Intervencije vođene medicinskim sestrama, poput planiranja otpusta, edukacije bolesnika, usklađivanja terapije te praćenja nakon otpusta, imaju za cilj spriječiti prekide u skrbi i smanjiti stopu ponovnih hospitalizacija.

Cilj: Ovaj sustavni pregled sintetizira novije dokaze o učinkovitosti tranzicijske skrbi vođene medicinskim sestrama kod odraslih bolesnika, s naglaskom na ponovne hospitalizacije, posjete hitnom prijemu, smrtnost, kvalitetu života i zadovoljstvo bolesnika.

Materijali i metode: Sustavnom pretragom baze PubMed za razdoblje od siječnja 2020. do rujna 2025. identificirana su randomizirana i kontrolirana istraživanja, opservacijske studije, protokoli s jasno definiranim ishodima te sustavni pregledi i metaanalize na engleskom ili hrvatskom jeziku. Primijenjeni su unaprijed definirani kriteriji uključenja i isključenja. Ukupno je pregledano 31 zapis, a 17 studija zadovoljilo je kriterije za uključivanje u analizu.

Rezultati: uključene studije pokazuju da tranzicijska skrb vođena medicinskim sestrama često smanjuje neplanirane ponovne prijeme u bolnicu, poboljšava kontinuitet skrbi te doprinosi većoj kvaliteti života i zadovoljstvu bolesnika. Najveća korist zabilježena je kod starijih osoba, bolesnika sa zatajivanjem srca te kod pacijenata nakon sepse ili cerebrovaskularnog infarkta. Modeli podržani telezdravstvom pokazali su se izvedivima i prihvatljivima. Učinak na smrtnost i učestalost posjeta hitnom prijemu bio je neujednačen, a jedna ekonomska analiza ukazala je da kompleksan tranzicijski program nije bio troškovno učinkovit.

Zaključak: Dostupni dokazi upućuju da tranzicijska skrb vođena medicinskim sestrama može unaprijediti ishode nakon otpusta i iskustvo

bolesnika, no njezina učinkovitost ovisi o rizičnom profilu bolesnika, sastavnicama intervencije i organizacijskom kontekstu. Za zdravstvene sustave poput hrvatskog, strukturirani modeli tranzicijske skrbi mogu doprinijeti smanjenju ponovnih hospitalizacija i učinkovitijem korištenju resursa, ali su potrebna dodatna pragmatična i ekonomska istraživanja.

Ključne riječi: tranzicijska skrb, intervencije vođene medicinskim sestrama, bolnički otpust, kontinuitet skrbi, ponovne hospitalizacije, ishodi liječenja

INTRODUCTION

Transitional care refers to a set of services and activities designed to ensure continuity of care during a patient's transfer between different levels or settings of healthcare, such as from hospital to home care (1). It extends beyond simple hospital discharge planning and includes coordinated, time-limited interventions that prevent gaps in care and enable the safe and timely handover of patients from one setting to another (2,3). In modern healthcare systems, reducing unnecessary hospital readmissions has become an important indicator of care quality (4).

Many countries have introduced policies and incentives to decrease readmission rates, ranging from financial penalties for hospitals with high readmission rates to the public reporting of quality indicators (5,6). The reason for this emphasis is the recognition that a proportion of readmissions is not inevitable but results from suboptimal discharge processes or inadequate communication between hospital and community-based care (7). Therefore, transitional care, delivered during the vulnerable period surrounding hospital discharge, is considered a key strategy for improving patient outcomes and optimising healthcare costs.

Nurses are often the primary providers of transitional care interventions. Nurse-led transitional care includes detailed discharge planning, patient education for self-management, medication reconciliation (for example, reviewing prescribed

medications at discharge), arrangement of follow-up contacts such as telephone calls or home visits, and coordination between hospital teams, primary care, and community services (8).

A substantial body of evidence shows that such programmes can improve patient outcomes by reducing unplanned readmissions and emergency visits, lowering mortality, and enhancing quality of life, while also generating potential cost savings through decreased rehospitalisation (9–13). For example, systematic reviews consistently demonstrate that transitional care, particularly when multicomponent in nature (such as symptom monitoring, education, and structured discharge planning), reduces the risk of readmission and overall healthcare costs, increases patient satisfaction, and may be cost-effective in specific contexts (1,14,15).

In the Croatian healthcare system, transitional care as a structured programme, similar to those implemented internationally, is not yet widely established. Hospital discharge in Croatia typically consists of a written discharge summary and a recommendation to follow up with a primary care physician, with the availability of community nursing or home care services in selected cases. However, a unified national model of nurse-led transitional care has not been developed, and the transition from hospital to community services often depends on the initiatives of individual institutions or project-based activities. Given that high readmission rates also pose a burden within the Croatian context, particularly among patients with chronic diseases and older adults, there is growing interest in introducing integrated programmes that would strengthen continuity of care.

AIM

The aim of the paper was to examine the most recent evidence (2020 to 2025) on the effectiveness of nurse-led transitional care interventions for adult patients. The focus is on outcomes such as hospital readmission rates, emergency department visits, mortality, quality of life, and patient satisfaction. This systematic review summarizes the interventions

that have been tested, the populations to which they were applied, and the outcomes they produced, and discusses the implications of the findings, including considerations relevant to the Croatian healthcare system.

MATERIALS AND METHODS

A systematic literature review was conducted in accordance with the IMRAD structure, covering the period from January 2020 to September 2025. The data source was the PubMed (MEDLINE) database; other databases were not searched, which represents a limitation of this review.

The search strategy was developed in advance and applied consistently. The following Boolean expression was used: (“transitional care” OR “continuity of patient care” OR “care coordination” OR “discharge planning”) AND (“nurse-led” OR “nurse intervention” OR “nurse”) AND (“readmission” OR “emergency department” OR “quality of life” OR “patient satisfaction”). Filters were applied for publication years 2020–2025, language (English or Croatian), and the availability of an abstract or full text.

Inclusion and exclusion criteria were defined a priori and are presented in Table 1. Study protocols were generally excluded, except when they explicitly described nurse-led transitional care interventions and predefined clinical outcomes. Such protocols were included because they inform the design and anticipated effects of the interventions

Table 1 **Inclusion and exclusion criteria.**

Inclusion criteria	Exclusion criteria
Studies published between January 2020 and September 2025	Studies published before 2020
Original research articles and review articles available in English or Croatian, with an abstract or full text	Articles in languages other than English or Croatian; editorials, letters, commentaries, books, or conference abstracts
Clinical and review studies: randomized controlled trials (RCTs), controlled clinical trials, prospective or retrospective observational studies, systematic reviews, and meta-analyses	Case reports, low-quality meta-analyses, animal studies, or studies without an available abstract or full text
Study protocols that explicitly define nurse-led transitional care interventions and planned clinical outcomes (for example, readmissions, quality of life, continuity of care)	Studies including paediatric or neonatal populations; studies not related to transitional care (for example, chronic disease management without hospital discharge, acute emergency care without a transitional component)
Programme evaluations and/or pilot studies reporting quantitative outcomes (for example 30-day readmissions, emergency department visits, mortality, quality of life, patient or caregiver satisfaction)	Studies that do not include a nurse-led role in the intervention
Studies examining nurse-led transitional care interventions for adult patients (discharge, telehealth, home visits, palliative or post acute care) and reporting clinical or experiential outcomes	

A total of 31 potentially relevant records were identified in PubMed. After screening titles and abstracts, all records were assessed in full text. Following detailed evaluation, 17 studies were included, and 14 were excluded. The most common reasons for exclusion were an inappropriate population or context (n=5), inadequate study design (n=4, for example, protocols or implementation reports without clinical outcomes), absence of a nurse-led role (n=3), and focus on acute care or models without a transitional component (n=2). Two authors independently reviewed all records, and disagreements were resolved through consensus.

From each included study, data were extracted on authors and year of publication, study design, population and country, description of the intervention, and main outcomes. For systematic reviews and meta-analyses, summary effects reported by the authors were recorded. The term

“nurse-led intervention” is used as an umbrella concept encompassing all forms of transitional care in which nurses have a leading, coordinating, or facilitating role (for example nurse led, nurse coordinated, or nurse navigator models). As only one database was searched, a PRISMA flow diagram is not presented; however, the selection process is described in the text.

In addition to the included studies, two recent meta-analyses (9,10) are referenced in the Discussion to provide a broader context, although they were not part of the final analytic sample.

RESULTS

Table 2 Summary of Included Studies (2020–2025).

Authors, year	Study type	Aim	Country	Main findings
Verweij L. et al., 2021 (16)	Mixed methods – process evaluation	To assess the implementation and fidelity of the Cardiac Care Bridge (CCB) transitional care programme in older cardiac patients.	Netherlands	Moderate to good fidelity to key components, with identified barriers and variability; findings support interpretation of RCT outcomes.
Verweij L. et al., 2022 (17)	Economic evaluation alongside RCT	To assess the cost-effectiveness of the CCB transitional care programme in older adults.	Netherlands	Not cost-effective compared with usual care (higher costs without improved outcomes).
Taylor SP et al., 2022 (18)	RCT	To examine the effect of the nurse navigator STAR programme after sepsis on 30-day outcomes.	USA	Lower 30-day composite outcome (mortality or readmission) in the intervention group.
Seidenfeld J. et al., 2021 (19)	RCT – secondary analysis	To identify subgroups responding differently to a nurse-led transitional care intervention after emergency department visits.	USA	Heterogeneous effects highlight the need for personalised transitional care.
Seidenfeld J. et al., 2023 (20)	Qualitative evaluation within RCT	To explore veterans' experiences with transitional care aimed at reducing emergency department use.	USA	Strong emphasis on the nursing role in education and coordination.
Pozzar RA et al., 2024 (21)	Pilot RCT	To test the feasibility and acceptability of a nurse-led telehealth programme (BOLSTER) for patients with peritoneal carcinomatosis and caregivers.	USA	Intervention feasible and acceptable; potential for broader implementation.
Michael NA et al., 2025 (22)	Systematic review and meta-analysis	To evaluate the effect of nurse-led transitional care on quality of life, mortality, and readmissions among stroke survivors.	International	Significant improvements in quality of life; no consistent effect on readmissions or mortality.
Lou X. & Xu H., 2021 (23)	RCT protocol	To examine the effect of an emergency department nursing intervention on psychological symptoms, continuity of care, and self-care.	China	Protocol defines outcomes, including return ED visits after discharge.
Li M. et al., 2021 (24)	Meta-analysis of RCTs	To assess the effectiveness of nurse-led transitional care for heart failure patients on	China	Reduced all-cause and HF-specific readmissions and shorter hospital stay; effect on

		healthcare utilisation.		ED visits unclear.
Krzesiński P. et al., 2021 (25)	Observational	To evaluate nurse-led ambulatory care supported by non-invasive haemodynamic assessment after HF decompensation.	Poland	Improved haemodynamic assessment and therapy optimisation; inconsistent evidence for early readmission reduction.
Koontalay A. et al., 2024 (8)	Meta-analysis	To assess nurse-led HF transitional care and its applicability in low-resource settings.	Thailand	Reduced readmissions and mortality; confirmed applicability in low-resource environments.
Jepma P. et al., 2021 (26)	RCT	To evaluate the nurse-coordinated CCB model in older cardiac patients.	Netherlands	No reduction in unplanned readmissions or mortality at 6 months; important process-related insights.
Hansen TK et al., 2021 (27)	RCT	To compare an early nurse-led transitional care model with a geriatric team model in frail older adults.	Denmark	Nurse-led model showed higher 30-day readmissions; no difference in 90-day mortality.
Griffin JM et al., 2024 (28)	RCT	To assess nurse-led transitional palliative care on caregiver and patient outcomes.	USA	Improved caregiver outcomes and patient quality of life.
Elsener M. et al., 2023 (29)	Programme evaluation	To evaluate a telehealth transitional care programme improving access and coordination after discharge.	Switzerland/ USA	Reduced 30-day readmissions; improved continuity and access; implementation insights.
Baecker A. et al., 2020 (30)	Programme evaluation	To assess outcomes of an HF transitional programme in an integrated health system.	USA	The programme did not reduce overall 30-day readmissions; early follow-up (≤ 7 days) was associated with a lower risk.
Averbuch T. et al., 2024 (31)	RCT	To evaluate the nurse-led PACT HF model on 3-year outcomes among HF patients.	Canada	No difference in 3-year composite outcome or individual components; numerically fewer ED visits in women; higher sacubitril/valsartan use in intervention group.

Five randomized controlled trials (18,26-28,31) examined the effects of transitional care across different populations, including patients after sepsis, individuals with cardiac conditions, geriatric patients, and those receiving palliative care. One small pilot study (21) evaluated the feasibility and acceptability of a telehealth model in an oncology population. A published RCT protocol (23) was included because it clearly defined planned outcomes, although results are not yet available. Two additional studies, one secondary analysis (19) and one qualitative evaluation within an RCT (20), provided deeper insight into the heterogeneity of effects and patients' subjective experiences.

Three observational studies and programme evaluations (25,29,30) explored the impact of implementing transitional care in routine practice, highlighting reductions in rehospitalisations and the importance of organisational factors. Three systematic reviews and meta-analyses (8,22,24) synthesised evidence in populations with chronic heart failure and stroke survivors, confirming the robustness of findings across different health systems and time periods. In addition, one economic evaluation (17) and one process analysis (16) contributed to understanding cost-effectiveness and implementation fidelity.

The geographic distribution of studies shows that most research was conducted in the United States (18-21,28,30) and the Netherlands (16,17,26), with individual studies originating from Canada (31), Denmark (27), Poland (25), Thailand (8), China (23,24), and Switzerland (29). One review had an international scope (22). This diversity indicates that transitional care is a subject of interest in both highly developed healthcare systems and resource-limited settings, underscoring the universal relevance of nurse-led interventions for ensuring continuity of care.

DISCUSSION

The findings of this systematic review confirm that nurse-led transitional care interventions have considerable potential to reduce hospital readmissions, decrease emergency department use,

and improve patient quality of life. These results align with recent systematic reviews and meta-analyses showing favourable effects of structured interventions, particularly in chronic cardiac populations and among older adults (3,8-11,24). This conclusion is consistent with earlier but methodologically robust evidence in heart failure populations (12), suggesting stability of effect across longer periods and different healthcare systems. At the same time, the heterogeneity of outcomes across studies highlights the importance of context and implementation fidelity, as emphasised by Landi et al. (2024) and Collet et al. (2025) in their economic and configurational analyses (1,15).

Effects on rehospitalisation and emergency department use

Evidence consistently shows that nurse-coordinated transitional care reduces the risk of rehospitalisation, especially among patients with heart failure (8,12,24,25,30,31). For example, the meta-analysis by Li et al. (2021) demonstrated reductions in both all-cause and heart failure-specific readmissions and shorter hospital stays, although without a significant effect on emergency department visits (24). Similarly, Koontalay et al. (2024) reported benefits even in low-resource settings (8). The sepsis-specific STAR programme reduced the composite outcome of 30-day readmission or mortality (18).

However, contradictory findings also exist. The Cardiac Care Bridge programme in the Netherlands did not demonstrate benefit (26), and its economic evaluation showed that it was dominated by usual care, being more costly and less effective (17). These results support analyses indicating that effectiveness depends heavily on system and population characteristics (7,9,14).

Impact on mortality and long-term clinical outcomes

In chronic heart failure populations, the three-year follow-up in the PACT HF trial did not demonstrate a statistically significant reduction in the composite outcome or its individual

components, although signals were observed in specific subgroups (31). In contrast, the STAR programme for patients after sepsis showed a favourable 30-day composite outcome of readmission or mortality (18). Conversely, the meta-analysis among stroke survivors found no reduction in mortality (22), which is consistent with findings from geriatric RCTs indicating that outcomes are sensitive to the organisational model of care (27). Comparison with network meta-analyses (9) further suggests that mortality is a “harder” endpoint in transitional care and depends heavily on early detection of decompensation and the ability to initiate timely referral, which is more pronounced in heart failure and post-sepsis than in neurological rehabilitation.

Quality of life, patient experience, and caregiver burden

Improvements in patient quality of life were particularly evident among stroke survivors and in palliative programmes (22,28). Transitional care also reduced caregiver burden and increased patient satisfaction, as confirmed by qualitative studies exploring veterans’ experiences (20). The BOLSTER pilot study demonstrated high acceptability of a telehealth model, with patients and caregivers emphasising the importance of nurses’ empathy and availability (21). These findings are consistent with global evidence highlighting quality of life and satisfaction as important secondary outcomes of transitional care programmes (9,10).

Determinants of heterogeneity: system-level, population-level, and implementation factors

Differences in outcomes can be explained by multilevel determinants. At the system level, effectiveness depends on organisational structures and readiness for implementation (1,3,15). At the population level, meta-analyses show the greatest benefit among frail older adults and individuals with chronic conditions (10,11). At the implementation level, poor fidelity and overly complex models reduce effectiveness (16,25). This reinforces that transitional care is not universally effective but

requires careful targeting and high-quality implementation (1,9,15).

Key components of interventions and their relative contribution to outcomes

Core elements of effective programmes include discharge planning, medication reconciliation, early post-discharge communication, and continuous symptom monitoring (9,14,24). Multicomponent interventions, such as education, telemonitoring, and home visits, achieve better outcomes, while education alone is insufficient (13,19). Interventions that include caregivers appear particularly effective (28).

Telehealth modalities: feasibility, scalability, and acceptability

The COVID-19 pandemic accelerated the adoption of telehealth models, and recent studies confirm their high acceptability and feasibility (21,29). Telehealth-supported programmes allow scalability and cost efficiency, although the absence of direct clinical examination presents a limitation. Therefore, hybrid models combining telemonitoring with targeted home visits are recommended (9,20,21).

Economic evaluation and conditions for cost-effectiveness

The economic impact of transitional care is not uniform. Systematic and economic reviews indicate benefit when programmes effectively reduce readmissions and resource use (1,15), whereas complex models without clinical impact generate additional costs. For example, in the economic evaluation by Verweij et al. (2022), the CCB programme was more costly and less effective than usual care (that is, dominated), and therefore cannot be considered cost-effective (17). Efficiency is achieved by targeting high-risk groups and implementing appropriately streamlined components (15,30).

Implications, recommendations, and limitations

The findings of this review indicate a need to introduce structured nurse-led transitional care programmes within the Croatian healthcare system, where discharge processes are still largely limited to written documentation. Such programmes have the potential to reduce rehospitalisations, improve patient satisfaction, and support more efficient use of healthcare resources. However, the available evidence has limitations: heterogeneity across studies and the absence of research in the Croatian context challenge the generalisation of findings. Practical recommendations include targeted enrolment of high-risk patients, the use of telehealth modalities, and a multidisciplinary approach with clearly defined nursing coordination roles. Future research should include pragmatic randomized trials, cost-effectiveness evaluations, and qualitative studies incorporating patient and caregiver perspectives. Pilot projects within hospitals and primary care settings, such as for patients with chronic heart failure or after myocardial infarction, could generate local evidence and form the foundation for broader implementation of transitional care.

CONCLUSION

This review confirms the importance of nurse-led transitional care interventions in ensuring continuity of care after hospital discharge. The evidence suggests that such programs can improve clinical outcomes, enhance patient satisfaction, and support a more efficient use of healthcare resources. Although the effects vary depending on organisational context and implementation quality, transitional care clearly represents a promising model that requires systematic planning and adaptation to national needs. For the Croatian healthcare system, this implies that introducing structured nurse-led transitional care should become a strategic priority, accompanied by the development of guidelines, nurse education, and the establishment of conditions that support their coordination role. Such measures would help ensure the sustainability and quality of care, reduce the risk

of related complications, and strengthen patient trust in the healthcare system.

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Acknowledgements: The authors wish to express their gratitude to colleagues from clinical nursing and transitional care services whose professional insights and everyday practice experiences contributed to the refinement of this manuscript.

Ethical Approval: Not applicable. This review did not involve human participants, patient data, or animal research.

Conflict of Interest: The authors declare that they have no conflicts of interest related to this manuscript.

Funding: This work received no external financial support.

Use of Artificial Intelligence: Editorial and language assistance was supported through AI-assisted proofreading and formatting tools, while all interpretation, synthesis, and final content remain the full responsibility of the authors, in line with EASE recommendations on the transparent and responsible use of AI in scientific writing.

Quality of Life of Patients Before and After Disc Herniation Surgery

Kvalitet života pacijenata prije i poslije operacije diskus hernije

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ABSTRACT

Introduction: Disc herniation is a leading cause of lumbar pain syndrome, significantly impairing the physical, psychological, and social aspects of patients' quality of life. Operative treatment aims not only to relieve pain but to restore overall functionality, emotional stability, and social well-being.

Aim: to evaluate the quality of life and daily functional activities of patients before and after disc herniation surgery, and to identify the key physical, psychosocial, gender, and occupational factors influencing postoperative outcomes.

Materials and methods: A systematic literature review was conducted using relevant domestic and international scientific databases. The study analyzed 21 peer-reviewed articles published between 2019 and 2024. The reviewed studies primarily utilized standardized health-related quality of life (HRQoL) assessment tools such as the Short Form 36 Health Survey (SF-36), EuroQol-5 Dimensions (EQ-5D), and the Oswestry Disability Index (ODI).

Results: The analysis of the literature indicates a profound improvement in the quality of life following surgical intervention. Minimally invasive

procedures, such as percutaneous transforaminal endoscopic discectomy (PTED), showed superior outcomes in pain reduction and functional recovery compared to traditional open methods. Furthermore, patients with a shorter preoperative duration of symptoms (<3 months) reported significantly higher postoperative satisfaction. Gender and occupational demands were also found to heavily influence the rehabilitation trajectory.

Conclusion: Disc herniation surgery significantly improves patients' quality of life compared to the preoperative period. Early diagnosis, the application of minimally invasive surgical techniques, and comprehensive, personalized postoperative rehabilitation are essential for achieving the best clinical and psychosocial outcomes.

Keywords: disc herniation, quality of life, surgery, rehabilitation, systematic review

SAŽETAK

Uvod: Diskus hernija je vodeći uzrok lumbalnog bolnog sindroma koji značajno narušava fizičke, psihološke i socijalne aspekte kvaliteta života pacijenata. Operativni tretman nema za cilj samo ublažavanje bola, već i obnavljanje ukupne

funkcionalnosti, emocionalne stabilnosti i općeg blagostanja.

Cilj: procijeniti kvalitet života i svakodnevne aktivnosti pacijenata prije i poslije operacije diskus hernije, te identificirati ključne fizičke, psihosocijalne, spolne i profesionalne faktore koji utječu na postoperativne ishode.

Materijali i metode: Proveden je sistematski pregled literature korištenjem relevantnih domaćih i međunarodnih naučnih baza podataka. U istraživanje je uključeno 21 recenziranih radova objavljenih u periodu od 2019. do 2024. godine. Analizirane studije su prvenstveno koristile standardizirane upitnike poput SF-36, EQ-5D i Oswestryjevog indeksa invaliditeta (ODI).

Rezultati: Analiza literature ukazuje na značajno poboljšanje kvaliteta života nakon operativnog zahvata. Minimalno invazivne procedure, poput perkutane transforaminalne endoskopske discektomije (PTED), pokazale su superiorne rezultate u smanjenju bola i funkcionalnom oporavku u poređenju sa tradicionalnim otvorenim metodama. Nadalje, pacijenti s kraćim preoperativnim trajanjem simptoma (<3 mjeseca) prijavili su znatno veće postoperativno zadovoljstvo. Spol i profesionalni zahtjevi radnog mjesta također su se pokazali kao faktori koji snažno utiču na tok rehabilitacije.

Zaključak: Operacija diskus hernije značajno poboljšava kvalitet života pacijenata u odnosu na preoperativni period. Rana dijagnoza, primjena minimalno invazivnih hirurških tehnika i sveobuhvatna, personalizirana postoperativna rehabilitacija od suštinskog su značaja za postizanje najboljih kliničkih i psihosocijalnih rezultata.

Ključne riječi: diskus hernija, kvalitet života, operativni zahvat, rehabilitacija, sistematski pregled

INTRODUCTION

Quality of life (QoL), as a comprehensive concept, has become a vital indicator of the success of medical treatments, particularly in the context of chronic diseases that significantly impact a patient's

daily functioning. A World Health Organization (WHO) expert group defined quality of life as an individual's perception of their position in life within the context of their culture, value system, goals, expectations, and interests (1). This definition acknowledges that QoL encompasses a broad spectrum of aspects, reflecting a holistic approach that integrates physical health, psychological well-being, social relationships, and interaction with the environment.

Lumbar pain syndrome (LBS), with disc herniation as its most frequent etiology, represents a major challenge for the contemporary medical profession. Epidemiological data suggest that the prevalence of this syndrome reaches up to 84% in the adult population at some point in their lives, predominantly affecting the working-age demographic (between the third and fifth decades of life) (2). This condition exerts an exceptionally negative impact on the global economy due to direct treatment costs and indirect costs related to lost productivity and disability.

The physical manifestations of disc herniation are severe. Pain, radiculopathy, reduced mobility, and muscle weakness restrict everyday activities, making simple tasks like walking, sitting, or lifting objects excruciatingly difficult. In advanced cases, complications such as cauda equina syndrome can lead to a loss of bladder and bowel control, representing a medical emergency that can result in permanent disability if not treated promptly (3).

However, the consequences of disc herniation extend far beyond the physical realm. The chronic nature of the pain profoundly disrupts the patient's psychological equilibrium. Individuals often develop kinesiophobia (the fear of movement), which creates a vicious cycle: the fear of pain leads to inactivity, which in turn causes muscle atrophy and exacerbates the underlying spinal instability (4). Furthermore, the prolonged inability to participate in social and professional activities frequently triggers anxiety, depression, and a profound sense of helplessness and social isolation (5).

Surgical intervention for disc herniation is often

the most effective, and sometimes the only, method for alleviating nerve compression and restoring patient functionality when conservative treatments fail (6). Yet, the success of a surgical procedure is no longer measured exclusively by anatomical correction or localized pain reduction. Modern healthcare paradigms dictate that success must be evaluated through the lens of the patient's overall quality of life. Evaluating QoL before and after surgery provides a comprehensive insight into how successfully the treatment has facilitated physical recovery, psychological stabilization, and the social reintegration of the patient (7).

AIM

The primary aim of this study is to evaluate the quality of life and daily functional activities of patients before and after disc herniation surgery. Furthermore, this study seeks to identify and analyze the specific physical, psychological, and social difficulties that impact overall QoL, and to determine how postoperative outcomes differ based on variables such as gender, age, occupation, and the duration of preoperative symptoms.

MATERIALS AND METHODS

This research was structured as a systematic literature review. Scientific and professional papers published in relevant domestic and international scientific databases were utilized to gather comprehensive data on postoperative outcomes.

The primary focus during the selection process was placed on longitudinal, descriptive, and retrospective-prospective studies that evaluated patients using standardized health self-assessment questionnaires. To ensure the highest level of objective comparison, studies were included if they utilized widely recognized psychometric tools, specifically:

- **Short Form 36 Health Survey (SF-36):** A highly validated tool that assesses eight dimensions of quality of life, including physical functioning, bodily pain, general health, vitality, social functioning, and mental health
- **Oswestry Disability Index (ODI):** An instrument specifically designed to quantify the degree of functional disability in patients with lower back pain during everyday activities
- **EuroQol-5 Dimensions (EQ-5D):** A standardized instrument covering mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, often paired with a Visual Analogue Scale (VAS).

The data extracted from the reviewed literature were grouped according to the surgical methodology, the duration of preoperative symptoms, and the sociodemographic characteristics of the cohorts. The review encompassed 21 peer-reviewed scientific papers published strictly between the years 2019 and 2024 to ensure the contemporary relevance of the surgical and rehabilitative techniques discussed.

RESULTS

Out of the systematically reviewed literature, 21 studies met the rigorous inclusion criteria, focusing on the pre- and postoperative quality of life in patients with lumbar disc herniation. The temporal distribution of the analyzed literature is presented in Figure 1, demonstrating a steady and recent research focus on this topic globally.

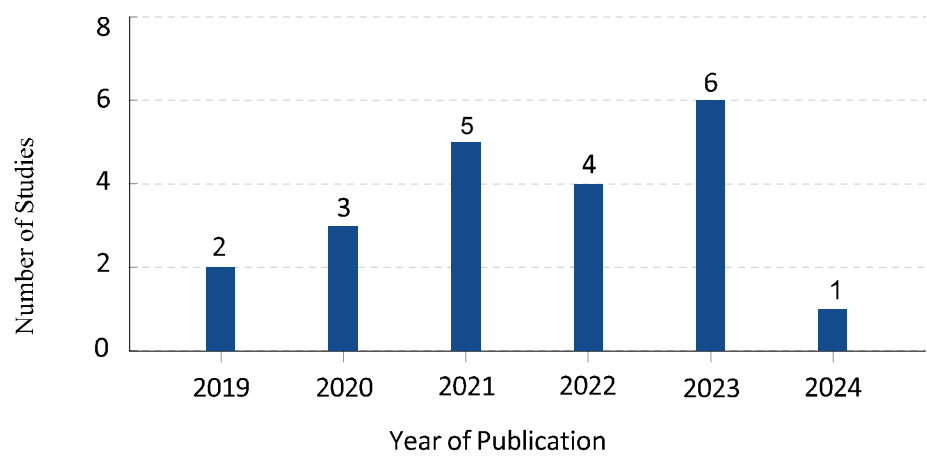


Figure 1 Distribution of the analyzed literature by year of publication.

The reviewed studies utilized various standardized tools to quantify clinical outcomes and subjective patient satisfaction. As illustrated in Figure 2, the SF-36 and the ODI were the most frequently deployed instruments, providing robust, comparable data across different international cohorts.

Impact of Surgical Techniques

The core findings regarding the efficacy of different surgical protocols indicate a massive shift toward minimally invasive spinal surgery. Studies focusing on Percutaneous Transforaminal Endoscopic Discectomy (PTED) and the TESSYS technique reported vastly superior outcomes compared to traditional fenestration discectomy. According to Zhao t, et al. (2023), PTED resulted in significantly lower postoperative VAS and ODI scores, indicating faster pain relief and less tissue trauma (8). Similarly, Zhou F, et al. (2021) demonstrated that endoscopic

procedures combined with targeted drug therapy significantly reduced serum inflammatory factors (IL-1 β , IL-6, TNF- γ), correlating directly with improved WHOQOL-BREF scores at 3 and 6 months post-operation (9).

Duration of Preoperative Symptoms

A critical prognostic factor identified across multiple studies was the duration of preoperative pain. Andersen et al. (2023) conducted a propensity-matched comparison which revealed that patients who underwent surgery within 3 months of symptom onset exhibited a highly significant satisfaction rate of 74.0%, alongside a 77.4% improvement in EQ-5D scores. Conversely, patients who endured chronic pain for over 24 months prior to surgery reported much lower satisfaction (48.7%) and a diminished overall QoL improvement (55.6%) (10).

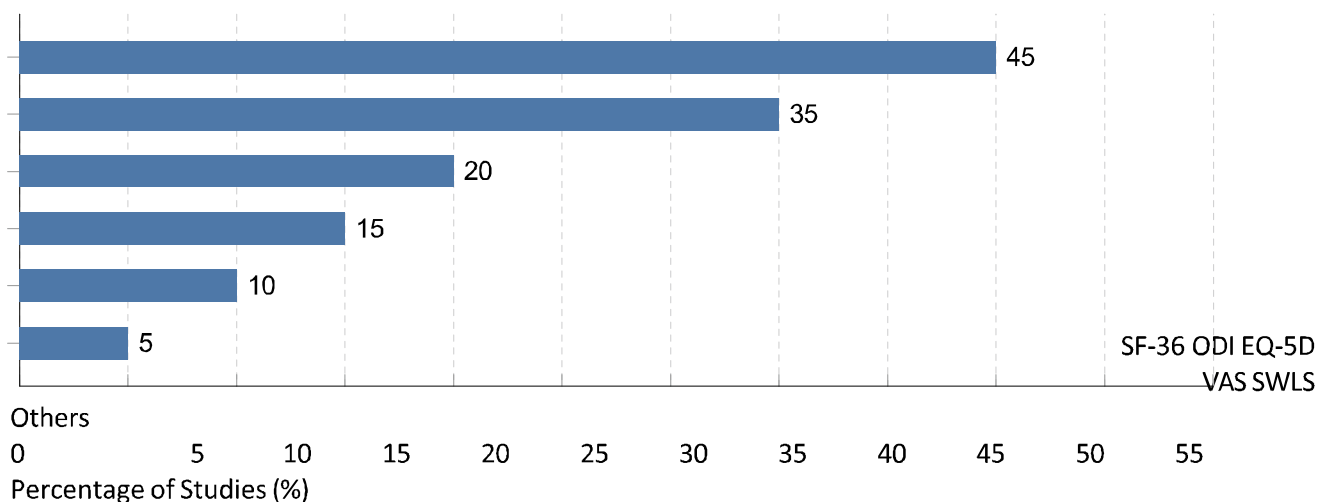


Figure 2 Frequency of QoL assessment instruments used in the reviewed studies.

Gender and Occupational Factors

The literature highlighted notable gender disparities in both preoperative suffering and postoperative recovery. Women systematically reported higher baseline pain intensities and a greater psychological burden, frequently associated with complex social and familial roles. Postoperatively, women exhibited a higher tendency toward reactive psychological states, scoring higher on hypochondriasis and sensitivity scales (MMPI-201 tests), necessitating more intensive psychological support during rehabilitation (11).

Occupation also played a definitive role. Patients engaged in heavy manual labor faced a significantly harder and longer reintegration into the workforce, reporting higher levels of frustration and lower SWLS (Satisfaction with Life Scale) scores compared to patients in administrative or intellectual roles, who benefited from the flexibility to manage their physical therapy schedules more effectively.

Postoperative Rehabilitation

The implementation of modern rehabilitation protocols significantly influenced QoL. The Enhanced Recovery after Surgery (ERAS) program, as studied by Wang et al. (2020), reduced the average hospital stay from 15.5 days to 12.3 days without increasing

complication rates. Furthermore, innovative approaches like pedometer-supported walking and telemonitoring, investigated by Aldemir K, et al. (2021), yielded significantly lower disability scores and vastly improved mental health and vitality dimensions on the SF-36 questionnaire by the third postoperative month (12).

DISCUSSION

The comprehensive review of contemporary scientific literature establishes unequivocally that quality of life is an indispensable metric for evaluating the success of disc herniation treatments. The transition of medical focus from purely anatomical restoration to a biopsychosocial model reflects a deeper understanding of the patient’s lived experience. Disc herniation severely restricts physical mobility, but its secondary effects, chronic pain, sleep deprivation, and the ensuing social isolation, can completely dismantle a patient’s psychological stability and economic independence. The findings of this systematic review confirm that surgical intervention significantly improves the quality of life for patients who are refractory to conservative treatment. As highlighted by Staszkievicz et al. (2023), surgical patients exhibit massive improvements on both the Satisfaction With Life Scale (SWLS) and the Oswestry Disability Index (ODI),

primarily driven by the immediate cessation of chronic radicular pain (13).

However, the data strongly suggests that the timing of the surgery is just as critical as the procedure itself. Andersen et al. (2023) demonstrated that prolonged preoperative suffering (exceeding 24 months) leads to entrenched central sensitization of pain and irreversible psychosocial

damage, which blunts the perceived success of the surgery. Patients operated on within the first 3 months of severe symptom onset reintegrated into their lives much faster and reported nearly double the satisfaction rates. This strongly challenges the traditional dogma of indefinitely prolonging conservative therapies when clear neurological indications for surgery are present.

Table 1 Summary of key reviewed studies on postoperative quality of life outcomes.

Author(s)	Year	Aim of the Study	Key Findings / Results
Wang P, et al.	2020	To investigate if the Enhanced Recovery After Surgery (ERAS) program improves QoL in elderly patients.	ERAS significantly reduced hospital stay (12.3 ± 3.03 days vs. 15.5 ± 1.88 days). Faster recovery noted without increased complications.
Zhao T, et al.	2023	To examine the safety and efficacy of percutaneous endoscopic discectomy (PTED) vs. traditional fenestration.	PTED yielded superior results in pain reduction (VAS) and disability (ODI). Postoperative scores were significantly lower than the traditional group.
Rapčan R, et al.	2023	To evaluate QoL changes in sciatica patients following endoscopic discectomy using EQ-5D-5L.	Surgery significantly reduced back and leg pain. EQ-5D dimensions improved significantly ($p < .001$), with sustained results 12 months post-op.
Staszkiwicz R, et al.	2023	To assess QoL, pain level, and disability outcomes after lumbar discectomy.	VAS pain levels decreased. Satisfaction With Life Scale (SWLS) increased.
Andersen MØ, et al.	2023	To examine the association between preoperative symptom duration and postoperative patient satisfaction.	Correlation found between baseline disc degeneration and final disability. Patients with shorter pain duration (<3 months) showed higher satisfaction (74.0%) compared to those with >24 months duration (48.7% satisfaction).
Aldemir K, et al.	2021	To determine the effect of pedometer-supported walking and telemonitoring on post-op pain and QoL.	Telemonitoring groups showed significantly lower pain/disability by month 3 ($p < 0.05$), with notable gains in mental health and vitality (SF-36).

The evolution of surgical techniques also plays a pivotal role in the speed and quality of recovery. Minimally invasive procedures (PTED, TESSYS) have proven to be game-changers (14). By minimizing collateral tissue damage and muscle stripping, these techniques reduce the immediate postoperative pain

that often hinders early physical therapy. When combined with ERAS protocols, the physiological stress of the operation is mitigated, allowing patients to begin mobility exercises almost immediately (15).

Finally, the postoperative phase requires a paradigm shift. The integration of digital health

tools, such as the telemonitoring and pedometer-based programs discussed by Aldemir K, et al. (2021), forces patients to take an active role in their rehabilitation. Furthermore, recognizing the distinct psychological and occupational burdens carried by different demographic groups, such as the heightened emotional stress in female patients or the vocational anxiety in heavy manual laborers, allows medical teams to deploy targeted psychological and ergonomic interventions, securing the long-term success of the surgical outcome.

CONCLUSION

Based on the theoretical framework and the empirical data analyzed in this systematic review, the working hypothesis is strongly confirmed: the quality of life and daily functioning of patients are significantly improved following disc herniation surgery compared to the preoperative period. Patients who undergo surgery, particularly those with a shorter duration of preoperative symptoms, report profound pain relief, higher subjective satisfaction, and superior functional recovery. The shift towards minimally invasive surgical techniques (such as endoscopic discectomy) has yielded exceptional results in minimizing postoperative disability and accelerating the patient's reintegration into social and professional life. However, achieving an optimal, long-lasting quality of life is not solely reliant on the surgical act itself. A holistic, multidisciplinary approach that integrates timely diagnosis, advanced minimally invasive methods, and comprehensives, personalized postoperative rehabilitation (including psychological support and modern telemonitoring) is absolutely essential to maximize both clinical and psychosocial outcomes.

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Authors' Contributions: AB and HK contributed significantly to the conception and design of the article, as well as the acquisition, analysis, and interpretation of data for the work. Each author had a role in drafting of the article and the revision process. Each author gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial Support and Sponsorship: nil.

Conflict of Interest: there are no conflicts of inter

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Should be concise and meet the objectives of the work, written in B/H/C and English language.

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ABSTRACT

Written in B/H/C and English language, containing a total of 200-250 words. Keywords are mandatory.

INTRODUCTION

The introduction is a short, concise part of the work containing the purpose of the work/problem in relation to other published works with a similar topic. It is necessary to define the problem, the aim of the research and/or set the work hypotheses. All is cited from the original literature.

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The main results of the research and the level of statistical significance should be quoted.

The results are presented in a tables or graphs, with clearly marked text and numerical notation.

The results must be statistically processed.

DISCUSSION

Discussion is concise and refers to own results which are then compared with other similar researches published in reference scientific databases. The discussion ends with confirmation or denial of the given goal or hypothesis.

CONCLUSION

It should be short and clear, mostly relate to crucial research data.

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