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Diagnostics of hemostasiological indicators of blood in patients with cervical cancer: standards, innovative models of the future (Ukraine)

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Abstract

This article focused on "Diagnostics of hemostasiological indicators of blood in patients with cervical cancer: standards, innovative models of the future (Ukraine)".

Aims: The aims of this study are to investigate the current standards, the innovative models, prognostic and predictive value of hemostasiological indicators of blood in patients with cervical cancer and identifications of potential gaps and opportunities in the current standards and innovative models for hemostasiological assessment.

Methodology: A descriptive cross-sectional study design was evaluated. Secondary data were collected. Descriptive statistics were obtained and utilised.

Results: The result showed that in 2020, Ukraine had 20.3 new cervical cancer cases per 100,000 women, regardless of age. Age-standardised cervical cancer incidence was 14.3 per 100,000 women. In 2020, Ukraine's lifetime cervical cancer risk was 1.4%. It illustrates cervical cancer risk. Prothrombin Time is 11–14 seconds, Activated Partial Thromboplastin Time is 25–35 seconds, fibrinogen is 200–400 mg/dL, and platelet counts are 150,000–450,000/L. Thromboelastography is a viscoelastic test that dynamically assesses blood clot formation, strength, and lysis. This test helps doctors assess cervical cancer patients' haemostatic profile and thrombotic risk and establish thromboprophylaxis regimens. In advanced cervical cancer patients, prothrombin time, APTT, fibrinogen, D-dimer, and platelet count predict thrombotic events and poor prognosis. These signs extend VTE risk. Potential gaps or opportunities include a lack of established practices, few complicated hemostasiological tests, little research, lack of knowledge and teaching, and difficulties with monitoring and follow-up, especially in resource-poor areas. Standardising techniques, expanding access to cutting-edge hemostasiological tests, and remote monitoring, and running education and awareness campaigns are future potentials for research and development.

Scientific Novelty: cutting-edge hemostasiological tests in cervical cancer.

Conclusion: In conclusion, resolving global cervical cancer mortality disparities needs healthcare, cancer prevention, screening, awareness, socioeconomic variables, and creative hemostasiological evaluation models. Better care, thromboprophylaxis, and collaboration can improve cervical cancer outcomes worldwide.

Keywords: cervical cancer; hemostasiological indicators; blood diagnostics; standards; innovative models; Ukraine

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Introduction

Cervical cancer is a type of cancer that affects the cervix, which is the lower part of the uterus that connects to the vagina. The human papillomavirus (HPV), which is passed from partner to partner via sexual contact, is the most frequent cause of cervical cancer. Regular screening exams, like a Pap test or an HPV test, which may identify abnormal cells in the cervix before they become cancerous, can often prevent cervical cancer. If aberrant cells are discovered, a course of therapy may be given to prevent them from developing into cancer. Abnormal vaginal bleeding, such as bleeding between periods or after sex, pelvic pain or discomfort, and atypical vaginal discharge are all potential symptoms of cervical cancer. Patients diagnosed with cervical cancer may see alterations in the hemostasiological (blood clotting) signs that are present in their bodies. The diagnosis of these indications is essential for determining the likelihood of bleeding or thrombosis (the process of blood clotting) and for directing decision-making about therapy. Platelet count, prothrombin time, and other typical hemostasiological markers are some of the things that may be assessed in people who have cervical cancer. These signs are able to be examined in the laboratory, and the results may assist medical professionals in determining the most appropriate course of therapy for people afflicted with cervical cancer.

Globally, it is the fourth most frequent malignancy in women. It is the most common cause of mortality among women. Statistics showed that about 90% of worldwide mortality in 2020 was attributable to new cases and deaths in nations with low or middle incomes. This highlighted the importance of this cancer. There are two human papillomavirus types, 16 and 18, and these are responsible for over 50% of high-grade cervical pre-cancers. Women with HIV are six times more likely to get cervical cancer than those without the infection. Primary prevention, early diagnosis, and prompt treatment help prevent cervical cancer at a fair cost. Cervical cancer may be cured if it is found early and treated well [1]. A chronic human papillomavirus infection in women is one of the key risk factors for cervical cancer. The cure rate for cervical cancer in women who get an early diagnosis varies from 80% to 95% [2–4].

In Ukraine, there are 20.1 million women who are at least 15 years old and at risk of developing cervical cancer. The illness now claims the lives of 2089 women annually, while 4756 other people are diagnosed with it. Cervical cancer is the fourth most prevalent cancer in women overall and the second most common cancer in women in Ukraine between the ages of 15 and 44. In spite of excellent screening and vaccination, invasive cervical cancer incidence and mortality have been steadily declining, yet it is still the most prevalent cause of death from cancer among women in Ukraine [5].

Cervical cancer is prevalent all over the world, especially in developing countries. 9.7% of women in the overall population of Eastern Europe are infected. Furthermore, cervical HPV-16 or 18 infections are accountable for 84.7% of invasive cervical cancers [6,7].

This is crucial to diagnosing a case, and the stage is decided for treatment purposes. The staging of cervical cancer is done using the International Federation of Gynaecology and Obstetrics classification of cervical cancer. Treatment is initially followed by a radical hysterectomy, which is then followed by radiation or chemotherapy, depending on the pathology report. However, the staging of cervical cancer can be unreliable, particularly in cases with advanced disease. Therefore, to categorise risks and direct therapies, accurate and available prognostic biomarkers are required. Currently, a number of serum indicators, including prothrombin time, aPTT, D-dimer, thrombocytosis, and haemoglobin, are being utilised to predict cancer progression [8–10]. In recent years, there has been a steadily growing amount of interest in the analysis of hemostasiological blood parameters in patients with cervical cancer. Prothrombin time, activated partial thromboplastin time, fibrinogen, D-dimer, and platelet count are some of the markers often used to evaluate cervical cancer patients' haemostatic status and anticipate thrombotic events [11–13].

The results of a retrospective investigation on patients with cervical cancer showed that a higher D-dimer level independently predicted an increased risk of venous thromboembolism. D-dimer levels and other clinical factors are taken into account by the Khorana grading system. In patients with cervical cancer and other cancers, this score system has been extensively used to determine the likelihood of venous thromboembolism (VT) and direct thromboprophylaxis strategies [14–16].

Rotational thromboelastometry (ROTEM) and thromboelastography (TEG) are point-of-care viscoelastic devices that evaluate fibrinolysis and coagulation using whole blood samples. Although these devices have undergone extensive research in cardiac surgery, there is only weak evidence to support their use in obstetrics. In addition to the current criteria of using common hemostasistical tests like PT, aPTT, several novel models have been proposed for the assessment of hemostasiological indicators of blood in cervical cancer patients in Ukraine. These models give new insights on the pathophysiology of haemostasis in cervical cancer and are intended to improve the precision and accuracy of hemostatic evaluation. A full assessment of the coagulation process,

including clot formation, clot strength, and fibrinolysis, is provided by the TEG, one of the viscoelastic tests. These aid in assessing the risk of venous thromboembolism (VT) and direct thromboprophylaxis techniques in the treatment of cervical cancer patients. [17–19].

The high cervical cancer incidence and mortality rates in Ukraine, especially among reproductive-age women, warrant the examination. Despite HPV vaccination and screening, cervical cancer is the leading cancer killer in Ukraine, underscoring the need for greater research and treatments. Ukrainian women are infected with high-risk HPV strains such as HPV-16 and HPV-18, highlighting the importance of blood hemostasiological indicators in cervical cancer patients. This study may alter cervical cancer treatment in Ukraine and other high-burden nations. Cervical cancer prognostic markers may help stratify risk and guide treatment in resource-limited settings. This study may also help develop standards for monitoring blood hemostasiological symptoms in cervical cancer patients in Ukraine to standardise clinical practise and improve patient care. In conclusion, a study on blood hemostasiological indicators in cervical cancer patients in Ukraine is warranted due to the high burden of the disease, the potential impact of haemostasis on patient outcomes, and the need for innovative models to improve hemostasiological assessment accuracy and precision. This work may help establish prognostic biomarkers, guidelines, and recommendations for cervical cancer management in Ukraine and other countries, improving patient outcomes.

Research Problem

Variability in criteria for blood hemostasiological markers, such as PT, aPTT, fibrinogen, D-dimer, and platelet count, may have an impact on the diagnosis and treatment of cervical cancer patients in Ukraine. Therefore, the research problem is:

1. To critically review the current standards for hemostasiological indicators of blood in patients with cervical cancer.
2. To identify the potential gaps or limitations and opportunities in the current practices.
3. To explore innovative models for the assessment of hemostasiological indicators of blood and evaluate their prognostic and predictive value in cervical cancer patients in Ukraine.

Research Focus

The focus of this study is to evaluate critically the existing norms for hemostasiological markers of blood in patients with cervical cancer in Ukraine and to highlight new, creative models. The goal of the study is to assess these hemostasiological variables' prognostic and predictive significance in cervical cancer patients, including their ability to foretell thrombotic episodes and inform thromboprophylaxis plans. Additionally, the study will suggest future paths for clinical practice and research in this field and highlight any potential flaws or restrictions in the creative models and current standards for hemostasiological evaluation in cervical cancer patients in Ukraine.

Research Aim and Research Questions

Aims and objectives of research are to study:

1. The current standards for hemostasiological indicators of blood in patients with cervical cancer in Ukraine.
2. The innovative models that have emerged for the assessment of hemostasiological indicators of blood in cervical cancer patients in Ukraine.
3. The prognostic and predictive value of hemostasiological indicators of blood in cervical cancer patients, including their role in predicting thrombotic events and guiding thromboprophylaxis strategies.
4. The potential gaps or limitations and opportunities in the current standards and innovative models for hemostasiological assessment.

Research Questions

1. What are the current standards for hemostasiological indicators of blood in patients with cervical cancer in Ukraine?
2. What innovative models have emerged for the assessment of hemostasiological indicators of blood in cervical cancer patients in Ukraine?
3. What is the prognostic and predictive value of hemostasiological indicators of blood in cervical cancer patients?

4. What potential gaps or limitations and opportunities exist in the current standards and innovative models for hemostasiological assessment in cervical cancer patients in Ukraine?

Research Methodology

General Background

Particularly in Ukraine, where the disease ranks as the second most common condition among women between the ages of 15 and 44, cervical carcinoma is a serious public health problem. Blood hemostasiological signs are critical in the diagnosis and management of cervical cancer patients. Haemostasis is the complex process that governs blood clotting and requires a delicate balance of procoagulant and anticoagulant substances. Changes in hemostasiological parameters can increase the risk of thrombosis or bleeding, which can have serious clinical consequences for cervical cancer patients. The findings of this study could help to establish prognostic biomarkers, specifications, and recommendations for cervical cancer management in Ukraine and other comparable settings, resulting in better outcomes for cervical cancer patients.

Data Analysis

A descriptive cross-sectional study methodology was utilised. For the purpose of gathering data, a questionnaire was used. Using both online and offline techniques, secondary data was gathered for the questionnaire from official sources and public data. Both types of data (quantitative and qualitative) were gathered. The study results were shown in the form table. Qualitative data was presented in the form of frequencies or percentages. Qualitative data was shown in the form of nominal data. There was no data analysis and just a data comparison in the discussion part.

Research Results

Status of cervical cancer

The results in (Table 1) showed that the data on cervical carcinoma in Ukraine provide an overview of the disease's impact there, including the prevalence of new cases, fatalities, and overall risk of contracting the disease. They may be helpful for comprehending how cervical cancer affects the populace and guiding public health policies and measures to lessen the disease's burden.

Table 1. Ukraine's status in Cervical Cancer

Variables	Frequency
Crude Cervical Cancer Deaths	2,434 per 100 000 women
Proportionate mortality rate of CC to total deaths	0.44%
Age adjusted Death Rate	7.04 per 100,000 population
Cervical cancer incidence	20.3 per 100 000 women
Age-standardised cervical cancer incidence	14.3 per 100 000 women
Cumulative risk of cervical cancer, ages 0-74	1.4%
Cervical cancer mortality-to-incidence ratio	0.44

Source: Authors' development based on cervical cancer Ukraine 2021 country profile n.d.

The number of new cases of cervical cancer diagnosed was 20.3 per 100,000 women in Ukraine in 2020, without taking into account age differences or other factors. It reflects the overall burden of cervical cancer in the population while Age-standardized cervical cancer incidence was 14.3 per 100,000 women in 2020, similar to the crude incidence rate, but it is age-standardized, which means that it takes into account the age distribution of the population. It allows for comparison of cervical cancer rates between different populations or countries with varying age distributions. Cumulative risk of cervical cancer, among ages 0-74 were1.4% in 2020 represents the estimated lifetime risk of developing cervical cancer from birth until the age of 74 in Ukraine. It indicates the likelihood of a woman in Ukraine developing cervical cancer during her lifetime. Cervical cancer mortality-to-incidence ratio was 0.44 in 2020 represents the proportion of cervical cancer deaths compared to the number of new cases diagnosed in Ukraine in 2020. A lower ratio indicates a lower mortality rate relative to the incidence of cervical cancer, which may suggest better survival outcomes. Population-based cancer registry exists as of 2021 indicates that Ukraine has a population-based cancer registry, which is a database that collects and records information on cancer cases in a defined population. It is an important tool for monitoring cancer incidence,

mortality, and trends over time. Total female population in 2019 was 23,610,000 represents the total number of females in Ukraine in 2019, which is the population at risk for cervical cancer while total female deaths in 2019 were 300,000, which includes all causes of death, including cervical cancer. The absence of a government immunisation program and women's disinterest in routine screening and treatment are the main causes of cervical cancer in Ukraine. According to the most recent WHO statistics, 2,434 women in Ukraine died from cervical cancer in 2020, accounting for 0.44 percent of all fatalities. Ukraine is ranked #106 in the world by age-adjusted Death Rate (7.04 per 100,000 of Population). Click on the links below to review more causes of death, or choose the complete health profile [20,21].

In conclusion, the statistics on cervical cancer in Ukraine provide important information about the severity of the disease there. According to estimates from 2020, a woman in Ukraine had a cumulative risk of 1.4% of acquiring cervical cancer between the ages of 0-74, which represents her lifetime risk of contracting the disease. The death-to-incidence ratio for cervical cancer in 2020, which was 0.44, indicates a considerably lower mortality rate when compared to the incidence rate, which could indicate better survival results. Furthermore, a population-based cancer registry is essential for observing cancer incidence, mortality, and long-term trends in Ukraine. The lack of a government immunisation programme and the poor rates of compliance with routine screening and treatment among women are the country's two biggest problems, though. Addressing these issues is crucial for lowering the incidence of cervical cancer in Ukraine and enhancing women's health outcomes. Promoting routine screening and treatment as well as putting into place efficient public health initiatives like vaccination campaigns will help prevent cervical cancer and increase survival rates. Ukraine may take action to lessen the effects of cervical cancer and enhance the general health and wellbeing of its female population by addressing these issues.

Current standards for hemostasiological indicators of blood in patients with cervical cancer

Results (Table 2) demonstrated that the normal range of the prothrombin time test value is 11–14 seconds, which is the normal reference range and potential predictive value for routinely measured hemostasiological indicators of blood in patients with cervical cancer in Ukraine.

Table 2. Hemostasiological indicators of blood in patients with cervical cancer in Ukraine

Hemostasiological Indicator	Value
Prothrombin Time	11-14 seconds
Activated Partial Thromboplastin Time	25-35 seconds
Fibrinogen	200-400 mg/dL
D-dimer	< 500 ng/mL or negative result
Platelet count	150,000-450,000 platelets/μL

Source: Authors' development based on Journal of Experimental and Clinical Medicine n.d.

Prolongation may indicate weakened clotting factors involved in the extrinsic route of the coagulation cascade in conditions such as liver illness, vitamin K insufficiency, or DIC. The Activated Partial Thromboplastin Time reference range is typically 25 to 35 seconds. In diseases like haemophilia, von Willebrand disease, or DIC, prolongation may be a sign that clotting components involved in the intrinsic pathway of the coagulation cascade are impaired. The typical range for fibrinogen is 200–400 mg/dL. Abnormal levels could be a sign of DIC, consumptive coagulopathies, or liver illness, among other disorders. 500 ng/mL, or a negative result, is the D-dimer normal range. Increased levels could be a sign of continuous clot disintegration, which is found in diseases such as venous thromboembolism, or DIC. The range of normal platelet counts is 150,000–450,000/L. A few illnesses that may be suggested by aberrant counts are thrombocytopenia (with a low platelet count) and thrombocytosis (with a high platelet count) [22–24]. The haemostatic status of these patients can be assessed by their PT, aPTT, fibrinogen, D-dimer, and platelet counts. These indications can indicate liver illness, vitamin K deficiency, DIC, haemophilia, von Willebrand disease, consumptive coagulopathies, or thromboembolic events. These findings highlight the need for monitoring hemostasiological markers in Ukrainian cervical cancer patients to assess clotting function and identify coagulation abnormalities. These findings may affect cervical cancer treatment, including coagulation problems and thrombotic events. These hemostasiological indications can help cervical cancer patients identify and treat aberrant clotting issues early, increasing their prognosis. In conclusion, understanding the normal reference ranges and potential predictive values of hemostasiological indicators in

cervical cancer patients in Ukraine will help clinicians manage coagulation-related problems. These hemostasiological variables may affect cervical cancer patient outcomes, hence, more studies and clinical trials are needed.

The innovative models for the assessment of hemostasiological indicators of blood in cervical cancer patients

The result in (Table 3 summarises a few of the novel approaches that have been developed for the evaluation of hemostasiological markers of blood in Ukrainian patients with cervical cancer: a viscoelastic test called thromboelastography offers a dynamic evaluation of the entire blood clotting process, including clot formation, strength, and lysis. With the use of this test, doctors can better understand the haemostatic profile and thrombotic risk of cervical cancer patients and develop tailored thromboprophylaxis plans. The TEG parameters are examined by the TEG analysis software. The TEG parameters include R-time, which gauges how long it takes for the first fibrin to form after the test begins, K-time, which gauges how long it takes for the graph to amplify to 20 mm, angle, which gauges how quickly clots form, maximum amplitude, which gauges how strong clots are, with fibrinogen and platelets accounting for 20% and 80% of clot strength, respectively, and coagulation index, which is a calculated [25]. This innovative approach has also been applied to research on coagulopathy brought on by cancer [26] and has expanding clinical roles. 23 recommendations and 7 best practices for cervical cancer screening and treatment have been published by the WHO in a guideline [27].

Table 3. Innovative models for the assessment of hemostasiological indicators of blood in cervical cancer patients

Innovative hemostasiological Models
Thromboelastography (TEG)
Rotational thromboelastometry (ROTEM)
Microparticle-based assays
Global clotting assays (GCAs)

Source: Authors' development based on WHO n.d.

Rotational thromboelastometry is a different viscoelastic assay that may be helpful in determining the haemostatic condition and directing thromboprophylaxis in patients with cervical cancer. The traditional coagulation tests in vascular tissue surgery may be supplemented by this approach. This can be used in conjunction with TEG to foresee hypercoagulable conditions and thromboembolic consequences in cancer patients. Numerous studies indicate that ROTEM may be an effective technique for treating cervical cancer patients [28,29].

Microparticle-based assays are based on small vesicles produced by active or apoptotic cells. They are called microparticles, and they can be used as indicators of haemostatic and procoagulant activity in an assay. To measure the quantity and activity of procoagulant microparticles, such as tissue factor-positive microparticles, in cervical cancer patients, numerous microparticle-based tests have been created [30].

Global clotting assays (GCAs) are tests that offer a thorough evaluation of the blood's total clotting function and fibrinolytic activity. These tests take into account factors like clotting time, clot formation, clot strength, and clot lysis. This model aids in guiding thromboprophylaxis measures and offers vital information on the haemostatic status and thrombotic risk of cervical cancer patients [31].

It is very important to note that the comprehension of these innovative models or approaches should be done in conjunction with the clinical context, the characteristics of the patient, and any other relevant variables and should be based on validated reference ranges or guidelines that are specific to the population that is being studied. In order to determine the utility and therapeutic importance of these unique models for the assessment of hemostasiological variables in cervical cancer patients in Ukraine, additional research and validation studies may be required.

The prognostic and predictive value of hemostasiological indicators of blood in cervical cancer patients

The findings of a research study (Table 4) demonstrated the prognostic and predictive utility of hemostasiological blood markers in cervical cancer patients, as well as their function in foretelling thrombotic events and directing thromboprophylaxis techniques. Patients with advanced cervical cancer have a bad prognosis when their prothrombin time is high. a marker for individuals with cervical cancer who are at higher risk of thrombotic events. An elevated risk of VTE is indicated by prolongation, which may direct the use of thromboprophylaxis techniques. Patients with advanced cervical cancer have a bad prognosis when their

Activated Partial Thromboplastin Time is high, a marker for patients with cervical cancer who are at higher risk of thrombotic events. An elevated risk of VTE is indicated by prolongation, which may direct the use of thromboprophylaxis techniques.

Table 4. Prognostic and predictive value of hemostasiological indicators & their role in predicting thrombotic events and guiding thromboprophylaxis strategies:

Hemostasiological indicators	Prognostic Value	Predictive Value	Role in Thrombotic Events	Role in Thromboprophylaxis Strategies
Prothrombin Time	Advanced cervical cancer has a bad prognosis.	Cervical cancer patients' thrombotic risk predictor.	Prolongation raises VTE risk.	May advise thromboprophylaxis.
Activated Partial Thromboplastin Time	Advanced cervical cancer has a bad prognosis.	Cervical cancer patients' thrombotic risk predictor.	Prolongation raises VTE risk.	May advise thromboprophylaxis.
Fibrinogen	Advanced cervical cancer has a bad prognosis.	Cervical cancer patients' thrombotic risk predictor.	Prolongation raises VTE risk.	May advise thromboprophylaxis.
D-dimer	Advanced cervical cancer has a bad prognosis.	Cervical cancer patients' thrombotic risk predictor.	Prolongation raises VTE risk.	May advise thromboprophylaxis.
Platelet count	Advanced cervical cancer has a bad prognosis.	VTE risk increase with thrombocytopenia.	Prolongation raises VTE risk.	May advise thromboprophylaxis.

Source: Authors' development based on Journal of Experimental and Clinical Medicine n.d.

Patients with advanced cervical cancer have a bad prognosis when fibrinogen is present as a marker for patients with cervical cancer who are at higher risk of thrombotic events. An elevated risk of VTE is indicated by prolongation, which may direct the use of thromboprophylaxis techniques. Patients with advanced cervical cancer have a bad prognosis when they have high D-dimer levels. a marker for patients with cervical cancer who are at higher risk of thrombotic events. An elevated risk of VTE is indicated by prolongation, which may direct the use of thromboprophylaxis techniques. Patients with advanced cervical cancer have a bad prognosis when their platelet counts are high. Thrombocytopenia or thrombocytosis, or abnormal platelet counts, may signify a higher risk of VTE. An elevated risk of VTE is indicated by prolongation, which may direct the use of thromboprophylaxis techniques [32,33]. The Negative Predictive Value and Positive Predictive Value (PPV) are used to assess hemostasiological symptoms in cervical cancer patients in Ukraine. When a patient tests negative, there is a probability that they may not have the condition of interest. It demonstrates how a negative test result rules out the illness. A low-test result reliably eliminates the condition, according to a high NPV. The probability that a patient with a positive test result has the desired condition is known as PPV. A positive test result may predict the emergence of the disorder. A high PPV indicates that a positive test result is very reliable in confirming the diagnosis [34]. Hematological markers such as NLR, PLR, and RDW have been shown to have predictive value in patients with cervical cancer. In addition, studies have evaluated the prognostic value of micro vessel density in cervical cancer patients [35]. The results of the current investigation demonstrated the prognostic usefulness of pre-operative measurements of WBC, haemoglobin, lymphocyte, and platelet levels in patients with early cervical cancer. These findings imply that blood's hemostasiological markers might help cervical cancer patients plan their thromboprophylaxis regimens and forecast thrombotic occurrences [36].

In conclusion, advanced cervical cancer patients' thrombotic events and poor prognosis are predicted by the following blood tests: prothrombin time, activated partial thromboplastin time, fibrinogen, D-dimer, and platelet count. These symptoms increase the risk of VTE. These hemostasiological variables may help cervical cancer patients forecast thrombotic episodes and guide thromboprophylaxis. These findings suggest that hemostasiological indicators may help Ukrainian cervical cancer patients manage thrombotic risk. More research is needed to confirm this.

Potential gaps or limitations and opportunities

The findings of the research (Table 5) showed that there was a lack of standardized procedures, limited opportunities for advanced hemostasiological tests, limited research on hemostasiological assessment in cervical cancer patients, a lack of awareness and education, and difficulties in follow-up and monitoring of hemostatic function in cervical cancer patients, particularly in terms of resources. These are possible gaps and limitations within the current standards and innovative models for hemostasiological assessment of cervical cancer patients in Ukraine [36,37].

Table 5. Potential gaps or limitations and opportunities

Potential gaps or limitations	Opportunities
Lack of standardized protocols)	Standardization of hemostasiological assessment protocols
Limited access to advanced hemostasiological tests	Increased access to advanced hemostasiological tests
Limited research on hemostasiological assessment in cervical cancer patients	Conducting research on hemostasiological assessment in cervical cancer patients
Lack of awareness and education	Education and awareness campaigns
Challenges in follow-up and monitoring	Telemedicine and remote monitoring

Source: Authors' development based on Journal of Clinical Medicine 2020 n.d.

Standardising hemostasiological assessment protocols, creating standardised protocols for hemostasiological evaluation, and other opportunities for future research and clinical practise in this field Increasing access to cutting-edge hemostasiological tests, studying hemostasiological evaluation in cervical cancer patients, telemedicine and remote monitoring, education, and awareness campaigns Particularly in locations with limited resources, using telemedicine and remote monitoring technology can help patients with cervical cancer navigate the hurdles of follow-up and monitoring hemodynamic function while also enabling prompt detection and management of haemostatic abnormalities [38].

Despite the fact that hemostasiological assessment has demonstrated potential value in guiding thromboprophylaxis strategies and predicting thrombotic events in cervical cancer patients in Ukraine, there are a number of gaps and restrictions in the present standards and cutting-edge models for hemostasiological assessment in this population. These include a lack of established practices, few possibilities for complex hemostasiological tests, scant research, a lack of knowledge and instruction, and challenges with monitoring and follow-up, particularly in places with scarce resources. Standardising assessment techniques, expanding access to cutting-edge hemostasiological tests, leveraging telemedicine and remote monitoring, and running education and awareness campaigns are some future potentials for research and clinical practise in this area. These techniques might aid in addressing the shortcomings and enhancing hemostasiological evaluation in Ukrainian patients with cervical cancer, which would ultimately improve thrombotic risk management and patient outcomes.

Discussion

Status of cervical cancer

The statistics on cervical cancer in Ukraine contain information on the prevalence, mortality, overall risk, and mortality-to-incidence ratio of the disease. The prevalence of cervical cancer in the population is represented by the crude incidence rate of 20.3 new cases per 100,000 women in 2020, while the age-standardised incidence rate of 14.3 per 100,000 women adjusts for age disparities and enables comparisons between other groups. The low mortality-to-incidence ratio of 0.44 in 2020 and the cumulative risk of 1.4% for having cervical cancer by the age of 74 point to higher survival outcomes. With 2,434 fatalities from cervical cancer accounting for 0.44% of all deaths and an age-adjusted mortality rate of 7.04 per 100,000 people, Ukraine is ranked 106 internationally due to its rather high cervical cancer death rate. Turkey, on the other hand, has a lower death rate from cervical cancer, with 1,311 fatalities representing 0.34% of all fatalities and an age-adjusted death rate of 2.71 per 100,000 people, placing it at 153 internationally. This suggests that, when compared to Turkey, cervical cancer is a bigger public health concern in Ukraine. With 4,378 cervical cancer fatalities, or 2.11% of all deaths, and an age-adjusted death rate of 45.76 per 100,000 people, Uganda has the eighth-highest cervical cancer mortality rate in the world. This indicates that, compared to Ukraine and Turkey, cervical cancer is a major public health concern in Uganda, with a significantly greater burden [39].

In contrast, the United Kingdom has a lower cervical cancer death rate, with 1,099 deaths accounting for 0.21% of total deaths, and an age-adjusted death rate of 2.01 per 100,000 populations, ranking it at 165 globally. This indicates that cervical cancer is comparatively less prevalent as a cause of death in the United Kingdom. Uzbekistan has a moderate cervical cancer death rate, with 840 deaths accounting for 0.52% of total deaths, and an age-adjusted death rate of 5.68 per 100,000 populations, ranking it at 118 globally. Yemen has a relatively low cervical cancer death rate, with 119 deaths accounting for 0.08% of total deaths, and an age-adjusted death rate of 1.52 per 100,000 population, ranking it at 178 globally [40].

Cervical cancer is preventable and treatable, but it kills many people globally. The prompt's cervical cancer death rates and rankings show global differences. Access to healthcare, cancer prevention and screening

programs, cervical cancer education, and socioeconomic variables can affect these discrepancies. Healthcare access affects cervical cancer mortality. Low-resource countries may struggle to prevent and treat cervical cancer. Since early detection and treatment improve results, this may increase cervical cancer fatalities. Lack of screening programs, knowledge, and education on early detection, risk reduction, and healthy practises can empower people to prevent cervical cancer and seek urgent medical care. Poverty and inequality can increase cervical cancer fatality disparities. These gaps may necessitate extensive interventions that address social determinants of health and healthcare equity. This may include strengthening healthcare systems to ensure affordable and quality cervical cancer prevention and treatment services, implementing evidence-based screening and vaccination programs, promoting cervical cancer awareness and education, and addressing socioeconomic factors that contribute to health disparities.

Current standards for hemostasiological indicators of blood in patients with cervical cancer

Understanding the haemostatic condition of cervical cancer patients requires an understanding of the function of prothrombin in blood clotting and coagulation factors. One of the key components that helps blood clot is the protein prothrombin, which is produced by the liver. Clotting factors are a group of proteins that are necessary for normal clotting and must be present in appropriate amounts in order to sustain haemostasis Prothrombin time (PT) is frequently used as a coagulation test in clinical settings to evaluate the blood's capacity to clot. It is typically measured in seconds, and in healthy patients, the normal range is 10 to 14 seconds. Prothrombin activity is often expressed as a percentage, with a normal value above 70%. The International Normalized Ratio (INR), a standardized measurement of PT, is another metric frequently used to evaluate coagulation. In healthy people, the INR should fall between 0.8 and 1.2. The therapeutic interval for INR is typically higher in individuals undergoing oral anticoagulant treatment, ranging from 2.0–3.0 [41].

The assessment of patient treatment and patient prognosis benefited greatly from all of these tests. These tests are being used all around the world. It is noteworthy to note that individuals with cervical cancer have different coagulation properties compared to healthy individuals. This is something that should be kept in mind. A study that was conducted in India found that the levels of fibrinogen, prothrombin time, and activated partial thromboplastin time in cervical cancer patients were much higher than those seen in healthy control participants [42,43] .This shows the importance of using this test for prognosis.

Similar results were found in an Iranian, Korean, and Indonesian investigation, which found that cervical cancer patients had much higher D-dimer levels than healthy controls. As changed levels may indicate a procoagulant state, which may raise the risk of thromboembolic events, these findings imply that evaluating these coagulation parameters may be crucial in determining the haemostatic status of cervical cancer patients [44].

The complete blood count, which may assist in discovering possible prognostic indications for the course of the illness, is a crucial diagnostic tool for patients with cervical cancer. The changes in leukocyte and platelet counts following radiation may reflect the impact of cancer treatment on haematological parameters, whereas pre-treatment CBC may be a good predictive model for recurrence in early cervical cancer. These results underline the need for routine CBC monitoring in cervical cancer patients, as it may provide useful data for disease management and therapy choices. Coagulation parameter measurements, including PT, aPTT, fibrinogen levels, D-dimer levels, and CBC, may offer crucial information about the haemostatic condition of cervical cancer patients. A procoagulant condition or possible prognostic markers for the course of the disease may be indicated by altered values of these measures. Therefore, including these evaluations in the care of cervical cancer patients may help in developing suitable treatment plans and keeping an eye out for any potential coagulation disorder-related side effects. Additional information and suggestions for the management of coagulation parameters in cervical cancer patients may be provided by further study in this area.

The innovative models for the assessment of hemostasiological indicators of blood in cervical cancer patients

Recent years have witnessed substantial improvements in the evaluation of hemostasiological markers of blood in cervical cancer patients. These innovative models include like Thromboelastography (TEG), Rotational thromboelastometry (ROTEM), Microparticle-based assays and Global clotting assays (GCAs). These sophisticated haemostatic assays are being used in numerous nations throughout the world. Ukraine also benefited with these facilities but very limited. Ukraine has encountered difficulties while evaluating hemostasiological markers in cervical cancer patients due to a lack of resources and technological advancements. To evaluate the coagulation state of cervical cancer patients, researchers and doctors in Ukraine have been actively using cutting-edge models, such as TEG and other advanced haemostatic assays [45]. But cervical cancer patients, in developed nations, including the United States, Germany, the United Kingdom, and Italy, have been at the forefront of these developments. TEG has been widely used in the US to offer a thorough assessment of the coagulation state in cancer patients, especially those with cervical cancer, improving patient outcomes. The

use of TEG has allowed for a more accurate and personalised approach to managing haemostatic disorders in these patients, leading to improved patient outcomes [46].

Similar to this, nations in Europe like Germany, the United Kingdom, and Italy have also been actively using methods like TEG to evaluate coagulation parameters in patients with cervical cancer, enabling more accurate assessment of haemostatic state and customized treatment plans [47]. These innovative models in Italy have enabled a more accurate evaluation of haemostatic state, permitting customised treatment plans for cervical cancer patients in these nations [48].

There is no doubt that the examination of hemostasiological indicators in cervical cancer patients using novel models, such as TEG and other advanced hemostatic tests, has significantly improved patient outcomes in industrialised countries. These models provide a more precise and individualised method for treating haemostatic problems in these individuals, improving patient outcomes, and the use of TEG has made it possible to create treatment programmes that are specifically tailored to the haemostatic condition being assessed. But there are some points against this as well. The lack of resources and technological advancements has made it challenging for Ukraine to assess hemostasiological markers in cervical cancer patients. Furthermore, their access is still restricted, limiting their usefulness in enhancing patient outcomes. Despite hurdles, Ukraine has adopted these creative methods, focusing on cost-effectiveness, viability in resource-limited contexts, and responsiveness to population demands. Research and international collaboration can improve cervical cancer haemostatic evaluation and patient outcomes.

The prognostic and predictive value of hemostasiological indicators of blood in cervical cancer patients

The findings of the study indicate that hemostasiological indicators of blood in patients with cervical cancer have prognostic and predictive significance in predicting thrombotic events and guiding thromboprophylaxis techniques. This was demonstrated by the fact that the indicators were able to accurately forecast thrombotic occurrences [32,33]. This implies that these indicators can be useful in identifying patients at risk of developing thrombotic events and in designing appropriate thromboprophylaxis strategies to prevent such complications.

Studies have assessed the predictive usefulness of microvascular density in cervical cancer patients in addition to hematological indicators. Angiogenesis, which is a key factor in tumour growth and metastasis, is measured by microvascular density. Higher microvascular density has been linked to a worse prognosis in cervical cancer patients, and its examination can provide further data for outcome prediction and treatment strategy guidance [34]. Micro vascular density is a measure of angiogenesis, which plays a critical role in tumour growth and metastasis. Higher micro vascular density has been associated with poorer prognosis in cervical cancer patients, and its assessment can provide additional information for predicting outcomes and guiding treatment strategies.

Pre-operative assessments of white blood cell, haemoglobin, lymphocyte, and platelet levels have prognostic significance for prognosis in early cervical cancer patients, according to the results of the current study [35]. This shows that these hemostasiological blood markers may be helpful prognostic indicators in cervical cancer patients, assisting in the identification of those who are more likely to experience poor outcomes and thrombotic events [36]. The capacity of a given test to correctly anticipate the presence or absence of a certain disease or result is referred to as the test's predictive value. It is often given as a percentage and is determined by a number of variables, such as the test's sensitivity and specificity, the prevalence of the disease in the population being tested, and the likelihood that the condition would exist in the test subject prior to the test. Positive predictive value (PPV) and negative predictive value (NPV) are the two different forms of predictive values. In contrast, NPV is the likelihood that a negative test result will properly show the absence of the condition. PPV is the likelihood that a positive test result will accurately indicate the existence of the condition. The research also looked at negative predictive value (NPV), which is significant. The NPV calculates the chance that a certain outcome (such thrombotic events) won't happen in the case of a negative test result. A negative test result basically rules out the occurrence if the NPV is large. In the context of hemostasiological indicators of blood in cervical cancer patients, a high NPV would mean that a negative test result may be predictive of a low risk of thrombotic events, aiding in the appropriate direction of thromboprophylaxis strategies [19].

Overall, the study's findings underscore the importance of hemostasiological blood markers in cervical cancer patients for prognostic and predictive purposes. Haematological markers and measurements of angiogenesis are among the indicators that can be useful for forecasting outcomes, identifying patients who are more likely to experience thrombotic events, and directing thromboprophylaxis techniques in the treatment of cervical cancer patients.

Potential gaps or limitations and opportunities

The lack of standardised protocols, limited access to advanced hemostasiological tests, limited research on hemostasiological assessment in cervical cancer patients, a lack of awareness and education, and difficulties in follow-up and monitoring of haemostatic function in cervical cancer patients, particularly in resources, are possible gaps and limitations in the current standards and innovative models for hemostasiological assessment in cervical cancer patients in Ukraine [36,37]. Standardising hemostasiological assessment protocols, creating standardized protocols for hemostasiological evaluation, and other opportunities for future research and clinical practice in this field Increasing access to cutting-edge hemostasiological tests, studying hemostasiological evaluation in cervical cancer patients, telemedicine and remote monitoring, education and awareness campaigns: Particularly in locations with limited resources, using telemedicine and remote monitoring technology can help patients with cervical cancer navigate the hurdles of follow-up and monitoring haemostatic function while also enabling prompt detection and management of haemostatic abnormalities [38].

In a comparable circumstance, women who wanted to be screened for cervical cancer encountered minor obstacles such as ignorance and lack of access to information, high screening prices, low risk perceptions, and poor health-seeking habits. Unfavourable attitudes and behaviours are also influenced by social networks, sociocultural norms, men's roles, and HIV-related stigma when screening is included in HIV care. Macro-level barriers to cervical cancer screening were inadequate medical facilities and a dearth of national cancer prevention policies [49]. There were the same barriers and opportunities faced by women in Ethiopia as well [50].

Innovative models for hemostasiological assessment in cervical cancer patients in Ukraine and other countries should consider these potential gaps and limitations. Efforts should be made to standardise protocols, improve access to advanced hemostasiological tests, promote research and education, increase awareness among healthcare providers and patients, and address challenges in follow-up and monitoring. Addressing these limitations can help ensure the accurate assessment and management of haemostatic disorders in cervical cancer patients and improve patient outcomes.

Conclusions and Implications

Cervical cancer fatality rates vary worldwide. Healthcare, cancer prevention and screening programs, awareness and education, and socioeconomic factors contribute to these discrepancies. Following are the conclusions and implications of this study:

1. Cervical cancer mortality rates range dramatically between nations, with some bearing a heavier burden than others. Socioeconomic variables, cancer prevention and screening programs, awareness and education campaigns, and access to healthcare are all important contributors.
2. It may be possible to employ coagulation indices, as markers to evaluate the haemostatic status and prognosis of cervical cancer patients.
3. Patients with cervical cancer may show altered coagulation parameters, levels, indicating a procoagulant state and a possible increased risk of thromboembolic events.
4. Haematological variables may be used as potential prognostic markers for the course of the disease in patients with cervical cancer.
5. In affluent nations and Ukraine, cutting-edge models like Thromboelastography (TEG) and other sophisticated haemostatic assays are frequently used to evaluate hemostasiological signs in cervical cancer patients.
6. In spite of obstacles, Ukraine has advanced in implementing novel models for the evaluation of hemostasiological parameters.
7. Haematological markers offer prognostic and predictive utility in forecasting outcomes, increased risk of thrombotic events, and directing thromboprophylaxis techniques.
8. The current standards and models for hemostasiological assessment in cervical cancer patients in Ukraine and other nations may have potential gaps and limitations especially in settings with limited resources.

Implication:

1. The nations with higher cervical cancer death rates, policymakers and healthcare organizations need to provide priority to services for cervical cancer prevention and treatment.
2. To assess cervical cancer patients' risk of thromboembolic events and forecast disease outcomes, healthcare professionals should think about evaluating coagulation markers in these patients.

3. To identify patients with cervical cancer who are more likely to experience thromboembolic events, healthcare professionals should think about evaluating coagulation markers as part of their normal screening.
4. Tracking haematological variables in cervical cancer patients may help in determining if the illness will return or how well the treatment will work.
5. The use of cutting-edge haemostatic assessment models, such TEG, haemostatic problems in cervical cancer patients may be managed in a tailored and targeted way, improving clinical results and maybe lowering the risk of thromboembolic events.
6. The development of new models emphasises the necessity of adaptability and innovation in healthcare settings with constrained resources, as well as the possibilities for utilising local knowledge and cooperation to overcome obstacles and enhance patient care.
7. Clinicians can employ hemostasiological markers of blood in cervical cancer patients by identifying high-risk patients who can benefit from more aggressive thromboprophylaxis treatments and avoiding unnecessary interventions in low-risk patients, can enhance patient outcomes.
8. Filling in gaps and overcoming these constraints can have significant effects on the precise diagnosis and treatment of haemostatic disorders in cervical cancer patients.

In conclusion, resolving global cervical cancer mortality disparities needs healthcare, cancer prevention, screening, awareness, socioeconomic variables, and creative hemostasiological evaluation models. Better care, thromboprophylaxis, and collaboration can improve cervical cancer outcomes worldwide.

Author contribution

All authors have sufficiently contributed to the study and agreed with the results and conclusions.

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Ethical statement

This study does not require IRB approval as it does not involve human subjects/data.

Declaration of interest

No conflict of interest is declared by authors.

Data sharing statement

Data supporting the findings and conclusions are available upon request from the corresponding author.

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Acute renal failure in newborns in the practice of a pediatrician of the future

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Abstract

Aims: The treatment of an acute renal failure has not received much research in Kazakhstan, whether focusing on adults or children. As a result, there is a lack of awareness about the condition of the field's knowledge as well as its challenges and prospects. Thus the goal is to identify and assess the studies that are currently accessible concerning the treatment of acute kidney failure in newborns or infants in the context of Kazakhstan experience.

Study design: Literature review

Methodology: MEDLINE, Cochrane Reviews, and Pedro were among the databases used to conduct the literature search. The conjunctions "AND" and "OR" were used with certain keywords. The articles' time range was restricted between 2018 and 2022 in order to only present the most recent facts. Papers discussing acute renal failure in infants only in Kazakhstan were included in the inclusion criteria.

Results: Regarding the treatment of AKI in neonates in Kazakhstan, there are incredibly few available studies. The majority of trials involved individuals who were older. ESRD was more widely covered in conjunction with dialysis than AKI. Women are more prone to experience AKI turning into full-blown CKD.

Conclusion: To learn more about the state of acute renal failure in neonates in Kazakhstan, more field study is required. The frequency and prevalence of placing new-borns on dialysis should be updated and made publicly accessible. It is important to emphasise the causes and risk factors of AKI in babies of Kazakh ancestry in order to comprehend current trends.

Scientific Novelty: This is the first study that attempts to cover the status of pediatric acute renal failure management within Kazakhstan. It will serve as a starting point for prospective research on pediatric illnesses within the country, so as to understand where the health sector of Kazakhstan stands on the global stage.

Keywords: Acute kidney injury; Neonates; Kazakhstan; pediatric nephrologists.

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Introduction

An abrupt and frequently transitory loss of kidney function is referred to as acute renal failure (also known as acute kidney injury, or AKI). One regulatory system that is affected is the glomerular filtration rate, which in turn has an impact on a variety of other kidney-enacted regulatory systems like the renin-angiotensin system, erythropoiesis, hormone synthesis, etc. Dehydration, blood loss, drug use, infection, and urinary tract obstruction are just a few of the factors that might contribute to it [1]. AKI can cause consequences such as electrolyte imbalances, fluid overload, and a higher chance of developing chronic kidney disease (CKD) if it is not addressed. Dialysis is the only treatment option for end-stage renal failure, which is caused by untreated chronic kidney disease.

In the paediatric population, AKI can be particularly challenging to diagnose and manage. First of all, identifying infants with AKI is met with obstacles, which include infants exhibiting vague signs, including decreased urination, sluggishness, and poor eating. On the other hand, similar aetiologies such as dehydration, sepsis, and the use of nephrotoxic medications can cause AKI in older children. In the same vein, treating the underlying issue and offering supportive care are accompanied with managing AKI in kids. This could involve managing fluid intake, replacing electrolytes, and changing medication. If the child develops an end-stage renal disease, renal replacement therapy, such as dialysis, may be required in extreme situations. This is especially true for low birth weight or premature infants who ultimately end up with end-stage renal disease (ESRD) [2]. Even with dialysis, working with infants is difficult because of the immaturity of the renal tissue, as well as smaller vessel size and peritoneal space, which limits treatment options [3]. This is why researches into the management of AKI in new-borns are still an ongoing effort. This ongoing work is crucial as not only will it improve outcomes for this population but will also provide open up new venues into the management of kidney diseases as a whole. Particularly with regards to ESRD, innovative therapeutic measures and robust protocols can be devised to help in the treatment for infants with ESRD that necessitates dialysis. Since dialysis in a paediatric patient is met with numerous obstacles, the ongoing research may help overcome some of the challenges associated with dialysis in this population. In addition, providing support and resources for families of infants with ESRD can help them navigate the challenges of caring for a child on dialysis. This will also improve the impression patients have of their doctors, and further foster trust which forms a cornerstone in a successful healthcare setup. Collaborating with other healthcare providers and researchers can also help facilitate the sharing of knowledge and best practices for managing AKI and ESRD in new-borns.

In terms of newer approaches, recent studies have suggested that protocol-based strategies can help prevent and improve AKI in high-risk patients, such as those who are postoperative or in septic shock [1]. Additionally, new devices specifically designed to provide renal support therapy for neonates have been developed and are currently being tested [4]. These devices promise to enhance the ability to provide safe and reliable care to even the smallest infants.

Currently, it is unknown as to the extent of advancements or current strategies present regarding the management of AKI in the pediatric population within Kazakhstan. Overall, the healthcare system in Kazakhstan is largely owned and managed by the Kazakh Ministry of Health, and treatment is provided through a network of primary, secondary, and tertiary care facilities. At the same time, health insurance for Kazakh residents is mostly provided through the public sector government. But in terms of nephrology and urology within the health sector of Kazakhstan, very little information is available on AKI and its sequelae, chronic kidney disease (CKD) and end-stage renal disease (ESRD).

Currently, the literature shows a significant increase in the prevalence and incidence of ESRD on dialysis in Kazakhstan in 2014-2018 [5]. Despite this increase, there is a dearth of epidemiological data on ESRD within Kazakhstan. Even though chronic haemodialysis treatment has been available since 1974, the majority of public dialysis facilities are concentrated in large cities only, leaving access to the rural population difficult. However, legislative changes made in the early 2000s enabled the development of private dialysis centres across the nation, improving patient access to these facilities [5]. Will this alone be enough to rectify the core issue within the country with regards to dialysis to the pediatric population? It is still unknown what measures are being taken to address the lack of epidemiological data on ESRD within Kazakhstan, as this will open up to discourse on dialysis. Furthermore, it stands to question are there any initiatives to improve access to dialysis treatment for rural populations following the legislative changes? This query can only be satisfied by an on the field survey. Moreover, how do private dialysis centres compare to public ones in terms of quality of care and patient outcomes? If a discrepancy exists, then this points out to a bias in distribution of funding in the health sector. This can affect the majority of patients who come from poorer backgrounds.

For those suffering from CKD, according to the Global Burden of Disease Study, there were as many as 5.5% of the general population with CKD in 2016. This corresponds to a 44% rise in CKD cases between 1990 and

2016, which included 1600 deaths, or about 1% of all 2016 fatalities [6]. Regarding management, another study suggests that to decrease the burden of CKD in Kazakhstan, a comprehensive action plan with effective management of risk factors for CKD, improved screening among risk populations, and timely treatment is needed [7]. These figures indicate that a thorough action plan is required to address the prevalence of CKD in the nation, including efficient risk factor management, enhanced risk population screening, and prompt treatment. This also shows that in order to improve outcomes for people who have the illness, there may be gaps in the way CKD is currently managed in Kazakhstan, and thus, more research is warranted. The given article is only a brief overview of what is currently available, and more field research will be necessary in order to obtain comprehensive information on the management of renal diseases within Kazakhstan.

Research Problem

The management of renal failure, let alone renal failure in new-borns/infants, in Kazakhstan is a topic that has not been extensively studied. As a result, there is a lack of information on the current state of knowledge and the challenges and opportunities existing in this area. This presents a significant research problem as it limits the understanding of the needs and potential interventions that could improve the management of renal failure in Kazakhstan.

Research Focus

The focus of this literature review is to find and assess the currently available literature on the management of AKI in new-borns or infants within the setting of Kazakhstan. This review will include any type of study written in any language to ensure the inclusion of comprehensive information on the subject matter.

Research Aim and Research Questions

1. "What is the current state of knowledge regarding the management of renal failure in new-borns within Kazakhstan and what gaps exist in the literature that warrant further investigation?"
2. "What are the current challenges and opportunities in the management of renal failure in new-borns within Kazakhstan and how can these be addressed through targeted research and intervention efforts?"
3. "What innovation, framework, or novel strategy has been devised, if at all, for the management of renal failure in new-borns within Kazakhstan?"

Research Methodology

General Background

A literature search was conducted on several databases, including MEDLINE, Cochrane Reviews, and Pedro. Specific keywords with the conjunctions 'AND' and 'OR' were utilised, and these are displayed in Table 1. The time frame of the articles was kept among 2018-2022 so as to include only the latest data. The inclusion criteria included papers discussing acute renal failure or acute kidney injury in new-borns only within Kazakhstan. The exclusion criteria were renal diseases that did not look at AKI exclusively or at least did not determine aetiology or effects in the pediatric population. Also, papers published in a language other than English were excluded, but those published in Kazakhstan that had a translated portion were included. While this was not a systematic review, the authors felt an ordered approach to the search strategy was warranted to ensure a maximum number of articles found.

Data Analysis

Information sources:

- PubMed/MEDLINE (2000-2021)
- Cochrane/EMBASE (2000-2021)
- Pedro (2000-2021)

Data items:

- Author, Study type, Sample size, Gender ratio, Outcomes, Findings

Search strategy:

The search strategy is displayed in Table 1

Table 1. Search strategy on Pubmed

#	Query	Search Details	Results	Time
1	acute renal failure[Title/Abstract]	"acute renal failure"[Title/Abstract]	25106	14:50:07
2	acute renal failure[MeSH Terms]	"acute kidney injury"[MeSH Terms]	55386	14:50:30
3	((new-borns[Title/Abstract]) OR (infant[Title/Abstract])) OR (child[Title/Abstract])	"new-borns"[Title/Abstract] OR "infant"[Title/Abstract] OR "child"[Title/Abstract]	721364	14:51:35
4	neonate[MeSH Terms]	"infant, new-born"[MeSH Terms]	669188	14:52:37
5	Kazakhstan	"Kazakhstan"[MeSH Terms] OR "Kazakhstan"[All Fields] OR "Kazakhstan s"[All Fields]	8423	14:53:06
6	(acute renal failure[Title/Abstract]) AND (((newborns[Title/Abstract]) OR (infant[Title/Abstract])) OR (child[Title/Abstract]))	"acute renal failure"[Title/Abstract] AND ("new-borns"[Title/Abstract] OR "infant"[Title/Abstract] OR "child"[Title/Abstract])	669	14:53:39
7	((acute renal failure[Title/Abstract]) AND (((newborns[Title/Abstract]) OR (infant[Title/Abstract])) OR (child[Title/Abstract]))) AND (Kazakhstan)	"acute renal failure"[Title/Abstract] AND ("newborns"[Title/Abstract] OR "infant"[Title/Abstract] OR "child"[Title/Abstract]) AND ("Kazakhstan"[MeSH Terms] OR "Kazakhstan"[All Fields] OR "Kazakhstan s"[All Fields])	0	14:54:02
8	((acute renal failure[Title/Abstract]) AND (neonate[MeSH Terms])) AND (Kazakhstan)	"acute renal failure"[Title/Abstract] AND "infant, new-born"[MeSH Terms] AND ("Kazakhstan"[MeSH Terms] OR "Kazakhstan"[All Fields] OR "Kazakhstan s"[All Fields])	0	14:54:49
9	((acute renal failure[MeSH Terms]) AND (((new-borns[Title/Abstract]) OR (infant[Title/Abstract])) OR (child[Title/Abstract]))) AND (Kazakhstan)	"acute kidney injury"[MeSH Terms] AND ("new-borns"[Title/Abstract] OR "infant"[Title/Abstract] OR "child"[Title/Abstract]) AND ("Kazakhstan"[MeSH Terms] OR "Kazakhstan"[All Fields] OR "Kazakhstan s"[All Fields])	0	14:55:38
10	((acute renal failure[MeSH Terms]) AND (neonate[MeSH Terms])) AND (Kazakhstan)	"acute kidney injury"[MeSH Terms] AND "infant, new-born"[MeSH Terms] AND ("Kazakhstan"[MeSH Terms] OR "Kazakhstan"[All Fields] OR "Kazakhstan s"[All Fields])	0	14:56:20
11	(acute kidney injury[MeSH Terms]) AND (Kazakhstan[MeSH Terms]) - Schema: all	"acute kidney injury"[MeSH Terms] AND "Kazakhstan"[MeSH Terms]	0	14:59:00
12	(acute kidney injury[MeSH Terms]) AND (Kazakhstan[MeSH Terms])	"acute kidney injury"[MeSH Terms] AND "Kazakhstan"[MeSH Terms]	0	14:59:00
13	(disease, end-stage kidney[MeSH Terms]) AND (Kazakhstan[MeSH Terms])	"kidney failure, chronic"[MeSH Terms] AND "Kazakhstan"[MeSH Terms]	1	14:59:33

Research Results

Salient findings

1. Only three studies barely matched the inclusion criteria
2. Regarding the management of AKI in new-borns within Kazakhstan there is an extreme lack of studies.
3. The majority of the studies covered cases with older patients.
4. Compared to AKI, ESRD was more covered along with dialysis.
5. Females are more likely to be affected by AKI developing into full fledge CKD (Table 2)
6. Dialysis following AKI was not linked to CKD (Table 2)
7. Caesarean section was most associated with the development of AKI in new-borns with CHD (Table 2)

Synthesis of studies

The table below displays notable findings from studies that fell under our inclusion criteria.

Table 2. Synthesis of studies

Author	Study type	Sample (if applicable)	Gender ratio (if applicable)	Outcomes	Findings
Khvan, Galiyeva, Bamysh, Issakov, Nigmatullina, Altynova et al. 2019 [8]	Retrospective cohort	77	53% male	1. CBC 2. Length of anuria 3. Length of dialysis 4. Neurological complications	-5 patients died -7 patients developed CKD -3 needed permanent dialysis Haemoglobin < 6.5g/dL, anuria day of starting dialysis, and length of anuria > 10 days were not linked with developing CKD.
Sadykova AZh, Boranbaeva RZ, Sarsenbaeva GI, Sepbaeva AD, Zhovnir VA, Berdijarova GS, et al. et al., 2022 [9]	Retrospective	60	-	Perinatal risk factors for AKI in new-borns with CHD	The incidence of CHA AKI was 58.3% Perinatal risk factors: Caesarean section – 48.5% Foetoplacental insufficiency (FPI) – 14%, Critical condition of the foetus -11%
Gaipov, Issanov, Kadyrzhanuly, Galiyeva, Khvan, Aljofan et al., 2020 [5]	Retrospective cohort	8898 (100 below 18 years of age)	56% male (overall)	Prevalence incidence mortality rate	16% mortality of AKI patients (below 18 years of age) on dialysis While the mortality rate decreased over the years, females were associated with lower survival

Understanding AKI in newborns globally

Despite the lack of specific information available from Kazakhstan, the principles of AKI with regard to aetiology, signs/symptoms, investigations, and management in new-borns remain globally uniform. These are elucidated in the coming paragraphs.

The most prevalent causes of acute renal failure in new-borns include prerenal, intrinsic renal disease, and obstructive uropathy. Congenital conditions like renal dysplasia with or without the obstruction of the urinary tract and hereditary conditions like autosomal recessive polycystic kidney disease can cause renal failure in the infant with prenatal onset [10]. These are normally picked up early on, but the prognosis is poor.

In the postnatal period, hypoxic-ischemic injury and harmful substances are additional common causes of acute renal failure in new-borns. When used to treat a patent ductus arteriosus, aminoglycoside antibiotics and nonsteroidal anti-inflammatory medicines are frequently linked to nephrotoxic acute renal failure in new-borns. Almost half of the premature neonates who receive indomethacin develop altered renal function [11]. Although it should be kept in mind that these changes are typically reversible; so the use of these medicines should be determined after weighing benefit against harm.

Renal failure can develop from both bilateral renal artery thrombosis and unilateral renal vein thrombosis. Histologically, cortical necrosis is linked to hypoxic insults brought on by placenta abruption, twin-twin or twin-maternal transfusions, twin-twin or twin-maternal anoxia, and involvement of the coagulation cascade [12–14]. However, the discussion of the exact mechanism and pathophysiology goes beyond the scope of this study.

Similar to the acute renal failure in older kids, multiple causes of acute renal failure in infants are common. But all causes can put the infant at an increased risk of becoming critically ill. This is especially true for neonates, as acute renal failure is widespread in the neonatal intensive care unit [4, 15]. However, the exact incidence and frequency in new-borns remain unknown. To better understand and address this issue, it would be important to conduct further research to determine the exact incidence and frequency of acute renal failure in new-borns. Understanding the specific causes of acute renal failure in infants can help inform prevention and treatment strategies. Given the increased risk of critical illness associated with acute renal failure in infants, it is important for healthcare providers to closely monitor and promptly treat this condition. Additionally, families of infants with

acute renal failure may need additional resources and support to help them navigate this challenging time. For example, providing educational materials and resources can help families better understand their infant's condition and treatment options. Connecting families with support groups or organizations can provide emotional and practical support during this difficult time. Financial assistance or resources to help cover the costs of medical care and treatment can also be helpful. Additionally, access to counselling or mental health services can help families cope with the stress and emotional challenges of caring for an infant with acute renal failure. By providing these types of resources and support, healthcare providers and organisations can help families feel more empowered and supported as they care for their infant.

Once the inherent renal failure has been established, the management of the metabolic side effects of acute renal failure continues to entail appropriate control of fluid balance, electrolyte status, acid-base balance, and the start of renal replacement medication. Hemofiltration with or without a dialysis circuit, intermittent haemodialysis, or peritoneal dialysis are all options for providing renal replacement treatment [16]. Except for neonates and small children, paediatric nephrologists are increasingly favouring hemofiltration while reducing their usage of peritoneal dialysis. Although the latter becomes useful in vascular access maintaining it may be challenging in the new-born. Whether or not paediatricians in Kazakhstan have opted for this method remains unknown, but it remains a key treatment option.

Looking at the overall prognosis, the underlying cause of acute renal failure has a significant impact on the outcomes and course of treatment for new-borns with acute renal failure. Multi organ failure, hypotension, the requirement for vasopressors, hemodynamic instability, and the necessity for mechanical ventilation and dialysis are all factors that are linked to death. As previously mentioned, neonates are more prone to a higher risk of death, and one factor in this is multi organ failure resulting from acute renal failure [17]. Even if not apparent early on, the cortical necrosis can progress into full nephron involvement, leading to renal failure. Physicians can easily overlook this following the initial injury and management. Thus, to improve outcomes for new-borns with acute renal failure, it is important for physicians to closely monitor for signs of multi organ failure and other complications. This would require vigilance not just from the physician, but the attendants of the child as well, as sometimes they can pick up early signs, and merely have to convey those to the on-duty physician. Moreover, early identification and treatment of the underlying cause of acute renal failure can also help improve outcomes; this requires a firm grasp of the differentials of the signs resulting from AKI. Regarding the histology, additional research may be needed to better understand the progression of cortical necrosis into full nephron involvement and how this can be prevented or managed. This may fall outside the expertise of junior medical officers. But providing education and training opportunities for these junior physicians can help improve their ability to identify and manage complications associated with acute renal failure in new-borns.

Discussion

Perhaps the most glaringly obvious result from the given search was the absence of a sufficient number of studies. This is not entirely due to the narrowed search in terms of Kazakhstan population. It turns out few research has been conducted on AKI occurring in new-borns or pediatric patients in general. Despite the fact the neonatal survival has increased in recent years due to the advancements in neonatal-perinatal medicine, significant rates of mortality and morbidity still exist. All the obtained information is based on limited single-centre studies that often concentrate on a tiny fraction of the neonatal population.

Nevertheless, the information that is now available points to a significant incidence of AKI in asphyxiated new-borns, a high prevalence of non-oliguric AKI, and an overall poor prognosis for AKI [18–21]. Most other articles are limited to prospective studies with inadequate sample sizes and investigations and a lack of clear definitions. The lack of sample sizes may not be a fault on the study design but more of willingness of subjects within Kazakhstan. There may be a low interest to participate in studies or a negative perspective held by the public in participating in research. But without confirmation this is all conjecture, and a survey needs to be conducted in order to understand the public's interest to involve themselves in health activities or research. Awareness should be propagated about the benefits of participating in health activities and research work, as these will profit, not just the public, but the whole health sector of Kazakhstan in a long perspective.

When it comes to novel strategies or innovative approaches to managing AKI, the health sector of Kazakhstan can benefit from the newer research. New urine biomarkers have been found that can identify AKI within hours. Several of these indicators were first used in new-borns who needed cardiopulmonary bypass surgery. Unfortunately, there haven't been any evaluated studies to find AKI in new-borns with any cardiac illness, primarily because one of the most common causes of AKI is congenital heart disease. Even so, these biomarkers can aid in

diagnosing AKI and thus provide more effective therapeutic and preventative strategies for pediatricians within Kazakhstan.

Another interesting thing to note is how certain conditions that predispose to a higher risk of AKI should be kept in mind. This includes premature infants who are raised in an extra uterine environment. A study demonstrated how that is not ideal for glomerular development. There is growing evidence that premature new-borns are more susceptible to metabolic syndrome, chronic renal disease, and hypertension [22]. Consequently, CKD risk exists in premature new-borns with AKI. While it may be impossible to completely prevent the delivery of premature infants, the attending physician or nephrologist should be wary of the increased chances of mortality resulting from AKI. So the question arises, if a child is born prematurely, just what exactly of the extra uterine environment affects the new-born, and how can the effects be mitigated if at all? It merely boils down to the child's immunity to toxic insults, be they from drugs, germs, temperature changes, lack of fluid intake, etc. Each insult puts a strain on the kidney, further aggravating the child's condition and arresting development of the nephrons. It takes a concerted effort to tackle each and everything that can compromise the new-borns health, and this applies not just in a ward/ICU setting but also after discharge when the new-born is taken home. A regular follow-up is essential to ensure the kidneys are in working condition, but compliance by the parents/guardians plays a big part in this, as they are the ones who have to bring the new-born for the check-up. Currently, it is unknown as to the perspectives of parents of Kazakh children in bringing them to the pediatrician for regular check-ups. Do they prefer home treatment/remedies? Do they trust the physicians and surgeons? What part of healthcare are they satisfied with and what part are they disappointed with?

Ultimately, to address this research problem, the aims of future research could include conducting a comprehensive literature review to identify existing knowledge and gaps in the literature, as well as conducting primary research to gather new data on the management of acute renal failure in Kazakhstan. This could include surveys or interviews with healthcare providers and patients to better understand their experiences and needs. The ultimate goal of this research would be to inform the development of targeted interventions and policies to improve the management of acute renal failure in new-borns within Kazakhstan.

Conclusions and Implications

1. Detailed research is necessary in order to obtain additional data on the current status of acute renal failure in new-borns within Kazakhstan.

2. The incidence and prevalence of new-borns that perform dialysis should be updated and made available for public access.

3. The causes and risk factors of AKI in Kazakh ethnicity new-borns should be highlighted in order to understand current trends.

4. Current management should be compared and assessed with established guidelines to determine the efficiency of nephrologists within Kazakhstan.

5. More novel strategies should be developed to promote a culture of innovation and improve the outcomes for patients.

6. Health policymakers should take into account the lack of public available information regarding the hospitalisation rates of new-borns and the current status of AKI as a whole in the country.

7. Increasing collaboration between healthcare providers and researchers can help facilitate the sharing of knowledge and best practices for managing AKI in new-borns.

8. Providing education and training opportunities for healthcare providers can help improve their knowledge and skills in managing AKI in new-borns.

9. Developing and implementing standardised protocols for the diagnosis and management of AKI in new-borns can help improve the consistency and quality of care.

10. Increasing public awareness about the risk factors and prevention of AKI in new-borns can help reduce the incidence of this condition.

Prospects for further research

Since this is a foremost study that attempts to assess the current status of acute renal failure management of new-borns in Kazakhstan, this article can serve as a pioneer and an example for others to dive into investigating the current state of affairs within the health sector of Kazakhstan, particularly with regards to the pediatric

population, which are the most vulnerable. Prospective research can expand and cover management of other diseases that afflict new-borns and seek out any innovation by the Kazakhstan health sector that can be emulated by other countries.

Limitations

The study was unable to synthesise comprehensive information regarding the subject matter due to the lack of literature availability. One reason may be that much of the information has either not been published in journals yet or is not indexed in the top search engines. Moreover, since one did not include articles that were in a completely different language than English, it's possible that some of that information may have been missed.

Declaration

Author contribution: All authors have sufficiently contributed to the study and agreed with the results and conclusions.

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Cognitive impairment in arterial hypertension in Pakistan

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Abstract

Background: The main cause of death and disease on a global scale is high blood pressure, making it a critical issue for public health and a major public health concern.

Objective: This review will identify the available literature and conduct a study to determine the factors which are significantly connected with hypertension based cognitive impairment among the Pakistani population.

Methodology: Data was collected to evaluate the ramifications of this condition. The most significant element in hypertension-related cognitive impairment is the presence of risk factors, including socio-demographic factors, lifestyle hazards, and disease-based risks.

Results: Observational studies imply that therapy with antihypertensives is related to decreased instances of cognitive impairment.

Conclusion: There is a need for additional research to investigate these elements more in-depth and to compile global evidence on the subject.

Keywords: cardiovascular disease; cognitive disability; high blood pressure. treatment; management

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Introduction

There is a correlation between arterial hypertension and cognitive impairment. The key factors that are connected with cognitive disability in hypertension individuals include age, gender, education level, and the presence of other medical conditions. The likelihood of a patient experiencing cognitive impairment due to hypertension rises with the patient's age [1]. The link between blood pressure and cognitive function is mostly non-linear and can be altered by age, ethnicity, education level, and medications that lower blood pressure. The connection between hypertension and cognitive impairment is complicated and involves a number of brain mechanisms, but a full comprehension of this connection is essential for the maintenance of cognitive abilities in hypertensive patients [2]. It is compared to how high blood pressure affects a person's capacity to think, recall, or reason, but researchers are working hard to figure out the connection between the two. Cognitive decline is closely linked to hypertension. It has been observed that blood pressure-lowering medication has a beneficial effect on the preservation of cognitive ability, although the mechanism underlying this benefit is yet unknown [3].

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Patients who have hypertension absolutely need to have their blood pressure carefully monitored, brought under control, and treated in order to keep their cognitive abilities intact [4]. One study found that hypertension individuals performed poorly on neurocognitive measures like delayed recollection and regional prefrontal skills when equated to control group. The verdicts of neurocognitive testing revealed that hypertensive patients suffer from faulty cognitive abilities and memory loss. Hence, it was determined that these assays were sensitive enough and simple enough to employ in clinical settings [5]. Cognitive performance among young hypertensive patients on tests like attention/executive operating and memory was found to be significantly poor as compared to normotensive people. In contrast, the distinction in cognitive performance of middle-aged hypertensive people is not differentiated from normotensive without having to count, and both groups were independent of psychosocial, demographical, and alcohol-related factors [6]. The findings from different research have disclosed that cognitive performance between young hypertensive patients on tests like attention/executive operating and memory was found.

Research Problem

Elderly patients who have been reported to have mild hypertension and a slight impairment in their cognitive ability are in great danger of developing cardiovascular disease and intense cognitive decline. These patients need to be treated with antihypertensive therapy in order to avoid cardiovascular disorders and a further decline in cognitive function [7]. In industrialized nations, a substantial amount of research has been carried out to evaluate the connection between high blood pressure and cognitive impairment in relation to a variety of factors, including age, gender, educational attainment, and others. In addition, a comprehensive comprehension of the connection between the effects of various antihypertensive treatments for preventing impairments in cognitive ability has been achieved. Therefore this problem has been a sole focus of this project.

Research Focus

The current narrative review focuses on the extraction of studies from the literature review to identify the relation between hypertension and cognitive impairment, its risk factor, condition in Pakistan, current treatment and future perspective.

Research Aim

This review will identify the available literature and conduct a study to determine the factors which are significantly connected with hypertension based cognitive impairment among the Pakistani population

Research Questions

Does cognitive impairment have a significant relation with arterial hypertension in Pakistan?

What are the risk factors of cognitive impairment based hypertension?

What is the current measures of cognitive impairment based hypertension in Pakistan?

Research Methodology

General Background

The primary goals of a narrative review are to provide the author and the reader with a full overview of the subject matter, as well as to draw attention to major areas of research. Narrative reviews can serve to discover problems with the study and aid to improve and establish research topics. A first step in examining the data in a systematic manner and organizing them might be provided by means of a narrative synthesis. At the protocol stage, the procedures that will be used to conduct a narrative synthesis need to be explained. This is because a narrative synthesis will be utilized to a greater or lesser amount in a review.

Instrument and Procedures

Methodical Approach to the Search engines

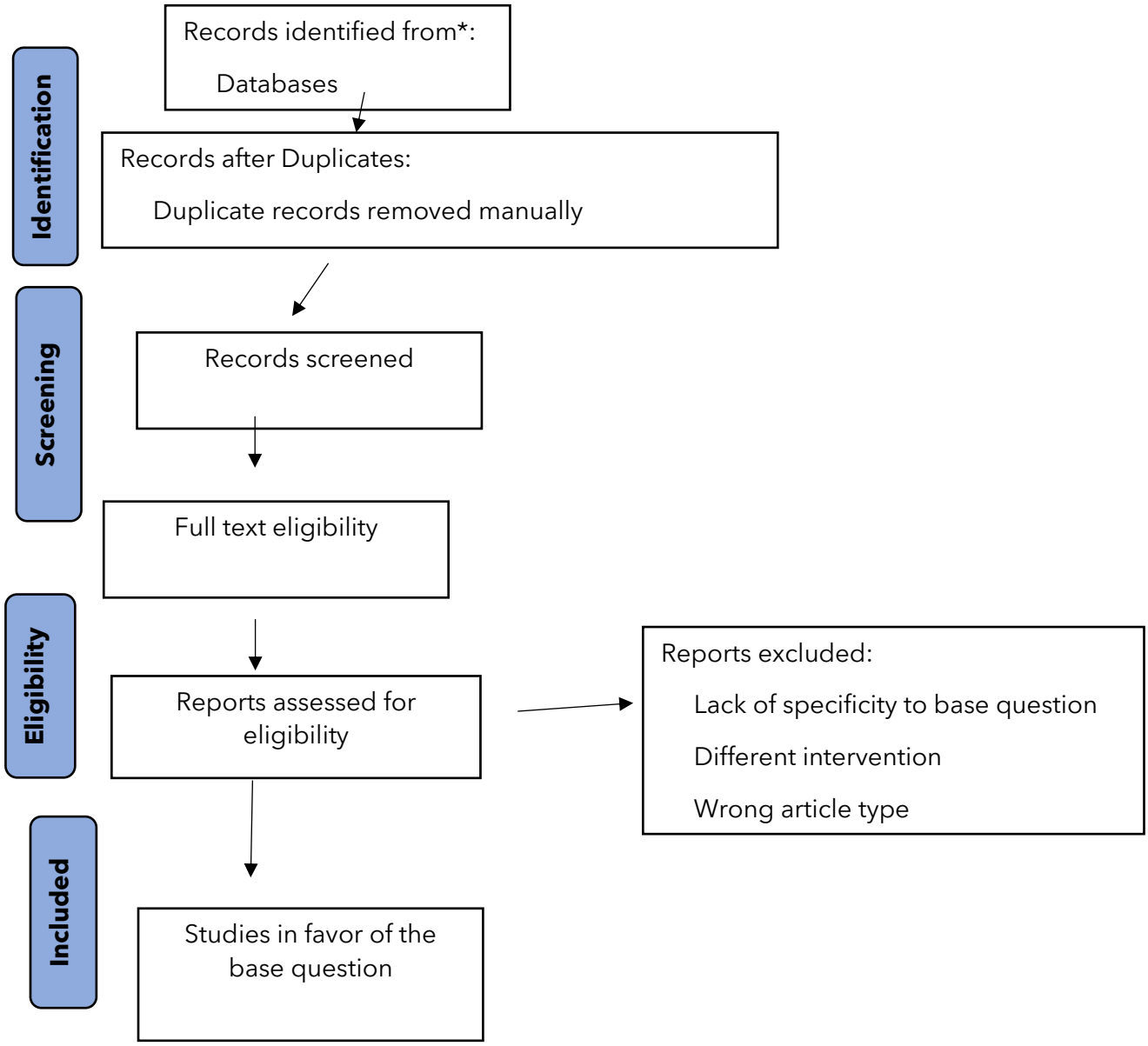
Data was collected from Google Scholar, PubMed, and the Medline database for articles available on the current topic. Both the articles' titles with abstracts consisting of keywords such as: blood pressure / hypertens / systolic / antihypertens / diastolic AND post-operative cognitive impairment / POCD / cognitive impairment AND mild cognitive impairment / MCI AND Pakistan studies. After the removal of duplicates, the remaining titles and abstracts of papers were examined by a single investigator to determine whether or not they met the inclusion criteria. The complete texts of the studies were accessed only if it was determined that they had the potential to meet the inclusion criteria or if it looked that they had data on both hypertension and cognitive.

Inclusion and Exclusion Criteria

Only studies that met all of the following requirements were considered for inclusion: i) an investigation into the potential of cognitive based hypertension ii) randomized controlled studuies of people with every age groups related to the topic iii) full text in the English language iv) ascertainment of blood pressure, hypertension, and its relation with cognitive impairement v) disclosing of these exposure factors with risk of cognitive impairment as relative risks among Pakistanis. Studies on hypotension or those showing correlation with other diseases weren't taken into consideration.

Data Analysis

The screening of the relevant data was the first step in the process of conducting the analysis of the data, which was then followed by the organizing the information that was extracted into a table. The articles that had been selected for further review were then evaluated one at a time in order to identify the overarching idea that most effectively illustrates the significance of the research question.



Literature overview

Pathogenesis of Hypertension

Essential hypertension has a complicated and extremely complex pathophysiology. The illness includes the interplay of various organ systems and encompass a wide range of independent or interdependent pathways, and the kidney is both a contributing organ and the target organ of the hypertensive phenomena. Genetics, activation of neurohormonal systems including the sympathetic nervous system and the renin-angiotensin-

aldosterone system, obesity, and high sodium consumption are all major factors in the development of hypertension. The condition of persistently elevated systemic blood pressure is known as arterial hypertension (BP). The sum of total peripheral vascular resistance and cardiac output determines blood pressure [8]. The tone of the sympathetic nerve system (SNS) and the parasympathetic neural system affects minute-to-minute fluctuations in blood pressure significantly [9]. Investigations utilizing continuous blood pressure monitoring have shown that the range of values on any given day can be distinct and exhibits a typical circadian pattern, in which blood pressure decreases at night or during sleeping, correlating with a reduction in SNS tone. Notwithstanding the fact that normal blood pressure is very variable, the majority of authorities describe increased hypertension as having a systolic blood pressure of less than 140 mmHg or a diastolic blood pressure of less than 90 mmHg, or both, measured when seated and relaxed [10].

When blood pressures are below 140/90 mmHg for more than 25% of measurements in any 24-hour period, hypertension is often considered to exist [11]. Just 5–10% of the US populace had blood pressure readings in that range when the 140/90 mmHg limit was chosen in the early 1900s [8]. Additionally, it was known from the beginning that hypertension in the hypertensive spectrum were almost always associated by small vessel disorder of the arterioles also known as arteriolosclerosis and kidneys that were massively contracted and "granular" in presence, with glomerular, and much more frequently tubular, modification on microscopic analysis [12].

Cognitive Impairment and its pathologic basis

One of the most prevalent clinical symptoms affecting the elderly is mild cognitive impairment (MCI), which is quickly rising in prevalence. It is unclear whether molecular and pathologic factors contribute to MCI in patients. It is crucial to describe the neuropathology alterations in the brains of patients who underwent autopsy with a well-defined diagnostic technique of MCI since MCI is a human-specific condition where neither clinical and nor neuropathological development appears to follow a clear linear route. A broad range of cellular molecular and biochemical deficits, many of which are related to cognitive impairment as well as compensatory reactions to the advancing disease process, must be considered when determining the pathologic substrate of MCI. These deficits must be considered in addition to the conventional plaque and coiled pathology. There may not be a singular incident that triggers this prodromal stage of AD due to the complexity of the neuronal detachment condition linked to MCI. In reality, at this point of the dementing chronic illness, it can be claimed that neuronal degeneration, which began at various stages of the neurological system, drives cognitive decline as a concluding common pathway [13, 14].

Research Results

By considering inclusion criteria in mind, 15 studies was extracted out. Some studies extracted the epidemiological of hypertension based cognitive impairment in Pakistan [15] and worldwide [16]. The results also identified the pathological relation between hypertension and cognitive impairment [17, 18]. Preclinical studies that have shown neuroinflammation among hypertension patient [19, 20]. Results alos demonstrated risk factors for hypertension based cognitive impairment include stress, smoking, disease based and age [21-30]. Research on hypertension based cognitive impairment data has been limited due to socio-economic factors. However, some studies [31-34] have demonstrated that there is a relationship between hypertension and cognitive impairment due to socio-demographic characteristics, comorbidities, or a previous history of hospitalization.

Table 1. The extracted information from screened studies

Extracted information	Reference
Hypertension is leading problem worldwide	[15]
Hypertension impairs several aspects of cognitive functioning	[16]
pathophysiological effects of hypertension-induced BBB disruption	[17, 18]
pathogen-based molecular sequences can enter the neural parenchyma through a disrupted BBB, where they induce neuroinflammation by activating microglia	[19, 20]
oxidative stress have directly role in neuroinflammation	[20]
risk variables include getting older, disease, stress, and smoking	[23]
Persistent stress is considered as an important factors that might donate to the onset of hypertension and other cardiovascular diseases.	[35, 36]

Underlie chronic stress's impact on hypertension and cognitive performance is an increase in the production of inflammatory cytokines by endothelial cells.	[37]
Tobacco use affects cognitive function and hypertension.	[38-41]
Smoking cause damage to the heart muscle, brain cell and cognition.	[42-47]
Diabetes has role in the progression of hypertension and cognitive diease	[24, 29, 30]
Estrogen-induced central suppression of sympathetic outflow in the case of hypertension.	[48-52]
Antihypertensive drugs have an impact on hypertensive Pakistani patients' cognitive function	[31]
Hypertension and impaired cognitive performance have a significant impact in Pakistani patients aged 70 or older.	[53]
A Pakistan and US study with similar findings identified low socioeconomic status as the cause of cognitive impairment in older people	[32, 33]
Cognitive impairment leads to depression among hypertenion's patients	[34]
Having hypertension have a huge impact on the quality of lifestyle and cognitive activities	[50-52]
Diuretics, dihydropyridine calcium channel blockers (CCBs), and inhibitors of the renin-angiotensin system can be helpful against cognitive impairment based on hypertension.	[54-56]
Pharmacological-based treatment of hypertension could result in a decline in cognitive impairment	[57]

Discussion

In order to prevent and treat age-related cognitive impairment (also referred as ARCI), it is important to have a thorough understanding of the interrelated risk factors, particularly how a person's genetic makeup affects their risk. Those who have heart illness or hypertension are at higher risk of developing aortic arch calcification. Moreover, a majority of the risk factors linked to the emergence of hypertension are also linked to the development of ARCI. These risk variables include getting older, disease, stress, and smoking [23].

Epidemiology

It is estimated that hypertension based adults aged prevalence of 65–74 year old in the United States is 76%, while the hypertension based adults aged prevalence of 75 years and above is 82%. In the 37 studies that were taken into consideration, the total prevalence of hypertension ranged anywhere from 3.0 to 77.5%. It ranged anywhere from 3.0 to 65.1% in research that used cross-sectional designs and from 27.5 to 77.5% in studies that used case-control designs. Even though more people are becoming aware of the harmful effects of hypertension, the rate at which blood pressure is controlled is still not as good as it could be [15]. At the end of the eighteenth century, the detrimental influence of hypertension on cognitive performance were identified [58]. Research conducted in the 1960s and 1970s gave evidence that hypertension impairs several aspects of cognitive functioning. After that, numerous prospective longitudinal investigations have shown that there is a significant connection among hypertennsion and the occurrence of cognitive impairment [16].

Pathophysiology basis of hypertension-based cognitive impairment

Cognitive decline is linked to lacunar infarcts, cerebral microhemorrhages, and white matter injury, are brought on by pathological changes in cerebral microvessels that harm the network signalling, microvascular structure, and function. Neuroinflammation, synapse loss, and impaired synaptic function are pathophysiological effects of hypertension-induced BBB disruption [17, 18]. IgG, fibrinogen, thrombin, and other inflammation of pathogen-based molecular sequences can enter the neural parenchyma through a disrupted BBB [18], where they induce neuroinflammation by activating microglia [19]. Preclinical studies that have shown that arterial rigidity causes microglia activation driven by oxidative stress have directly demonstrated the crucial role that haemodynamic variables play in neuroinflammation. Moreover, BBB disruption causes a rise in serum amyloid A levels in the brain, which plays a part in neuroinflammation with neurodegeneration [20].

Risk factors associated with hypertension-based cognitive impairment

Chronic Stress links to Blood Pressure and Brain Health: Persistent stress is considered as an important factors that might donate to the onset of hypertension [29] and other cardiovascular diseases [36]. It is well known that both short- and long-term stress can raise blood pressure by activating the sympathetic nervous system, which causes the sympathetic nerve terminals to produce norepinephrine. Vasoconstriction results from this, which also

activates the hypothalamic-pituitary-adrenal axis or HPA. The activation of the HPA leads to the discharge of corticotrophin-releasing factor (CRF) from neurons in the para-ventricular nucleus. As a result, the anterior pituitary releases more adrenocorticotropic hormone (ACTH), and the adrenal gland releases more catecholamines and glucocorticoids. Moreover, the mineralocorticoid aldosterone is released [24]. Endothelial cells lining blood vessels can endure long-term damage due to sustained shear stress if the HPA axis is continuously stimulated and activated. Damage of this kind leads to an increase in the production of inflammatory cytokines by endothelial cells, such as IL-6, C-reactive protein (CRP), IL-8, and PAI-1, as well as reactive oxygen species [ROS], which in turn causes modifications in vascular function, neovascularization, and the evolution of atherosclerosis [21, 22].

Smoking: It is also known that smoking leads to an increase in the amount of chronic inflammation that occurs in the vasculature as well as an increase in the number of cell adhesion molecules [38]. These two elements raise the risk of cardiovascular disease and hypertension, respectively. Increases in IL-6 levels, as well as aqueous ICAM-1 as well as MCP-1, have repeatedly been demonstrated to be strongly associated with cigarette usage [25, 26]. In the Framingham Heart Study, those who smoked had levels of soluble ICAM-1 that was 25% greater than nonsmokers [39]. Many research have been carried out to examine how long-term tobacco use affects cognitive function, and the majority of these studies have discovered a clear link between contemporary smoking and cognitive function [40, 41]. The connection between smoking and one's level of cognitive function was investigated over a span of 5.5 years in a study that involved 5705 individuals from the Rotterdam study [42, 43]. There are studies that suggest that the cellular mechanisms which are involved in the chronic effects of smoking on the damage done to the heart, blood vessels, and lungs are also involved in the damaging effects that smoking has on brain function and cognition [43]. This is in addition to the effects that smoking has on the cardiovascular and pulmonary systems. It has been established that smoking lowers performance on tests of executive function, memory and learning, attention, and processor speed [44]. These investigations were conducted on younger persons who did not have any underlying disorders that were readily apparent. According to magnetic resonance imaging (MRI) results, long-term cigarette smoking is substantially associated with reductions in gray and white matter volume and density [45, 46].

Diabetes: Throughout the past several decades, a significant amount of research has been conducted to investigate gender variations in the role that diabetes has on the progression of hypertension and cognitive diease [24, 29, 30]. Pre-menopausal women had a lower rate of hypertension as compared to men of the same age [59], despite the fact that both men-women have age-related rises in blood pressure as they get older. The risk of developing hypertension in women dramatically rises beyond the age of 55, with approximately 70 percent of women over the age of 65 in the United States being diagnosed with the condition. It is considered that premenopausal women who still have ovarian hormones in their bodies are provided some kind of defense against the risk of developing cardiovascular disease as well as high blood pressure [46, 47]. The idea that an estradiol-induced considerable increase in vascular endothelial nitric oxide secretion and vasodilation is one of the processes that contribute to ovarian hormone protection has been put forth as a possibility [48], improvements in endothelial function [49], and estrogen-induced central suppression of sympathetic outflow [50, 51] in the case of hypertension.

Cognitive impairment based hypertension in Pakistan

According to a study, antihypertensive drugs have an impact on hypertensive Pakistani patients' cognitive function [31]. Patients with hypertension taking beta-blockers had a higher percentage of cognitive impairment than patients taking diuretics, who had a lower percentage. Those receiving ACEI monotherapy and the calcium channel blocker/ARB combination also showed significantly less cognitive impairment than those receiving beta-blocker monotherapy. Similar studies have shown that calcium channel blockers and ACE inhibitors are more efficient than beta blockers as well as diuretics at postponing cognitive deterioration [48]. Although this link weakens with advancing age, cognitive loss or disability is strongly associated with elevated blood pressure, especially in a middle-aged sample [49]. The findings of the current investigation demonstrated that senior hypertensive patients who were older than 60 had a comparatively greater level of cognitive impairment. Similar results from a different study suggested a link between hypertension and impaired cognitive performance, particularly in patients aged 70 or older[53]. More literate adults had sharper minds than those who were less literate. The current investigation results indicated that low-educated hypertensive patients had a moderate level of cognitive impairment. Also, the current study found a link between hypertension patients' work status and cognitive function. It was shown that hypertension patients who had better-paying jobs and were employed exhibited superior cognitive function over those who were unemployed. When compared towards housewives of the same age, highly educated women in better professional positions displayed comparable signs of less cognitive deterioration. Furthermore, a strong correlation between the level of income and cognitive impairment was found in the current study. In patients with hypertension, lower income was associated with higher cognitive

decline. A Pakistan and US study with similar findings identified low socioeconomic status as the cause of cognitive impairment in older people [32, 33]. Another Pakistan-based research revealed the cognitive impairment leads to depression among hypertenion's patients. According to the findings, there is a relationship between hypertension and depression, and this association exists regardless of socio-demographic characteristics, comorbidities, or a previous history of hospitalisation [34]. Many research describe that participants having hypertension have a huge impact on the quality of lifestyle and cognitive activities [50-52].

Treatment

Because of the use of different drug combinations within and among trials, it is impossible to make conclusions in relation to individual drug classes. This is especially true when considering the low number of participants in the recently included research. It was hypothesised in the 1998 issue of Syst Eur that the neuroprotective properties of the CCB nitrendipine could make the prevention of dementia more feasible. According to the findings of one meta-analysis, diuretics, dihydropyridine calcium channel blockers (CCBs), and inhibitors of the renin-angiotensin system may have distinct effects on the body. Possible impacts that vary according to class have been discussed elsewhere [54-56], and additional research is now being conducted. These studies showed that pharmacological-based treatment of hypertension could result in a decline in cognitive impairment. It is essential to stress that cardiovascular outcomes, including cerebrovascular outcomes, were the primary objectives in the vast majority of the research investigations included in this analysis, with cognitive function and dementia serving as secondary endpoints. After it became clear that there would be improvements for the key endpoints, the previous trials were stopped. It is probable, as a result, that significant effects on cognitive control were not observed before the improvements in cardiovascular health became apparent [57].

Current situation and future perspective

Working in public health in identifying patient populations that are at high risk and in developing appropriate treatment and prevention methods. It is necessary to do more study in order to investigate the direct and indirect validating assumptions that relate particular important denominators with hypertension. The prioritization of medical treatment for hypertension patients residing in Pakistan will be made possible as a result of this, which is a significant step towards accomplishing the objective and will help bring Pakistan closer to its goal. The research also underlines the low quality of the evidence that is currently accessible, particularly with regard to the subject of hypertension and broadly speaking with regard to the overall research and policy on healthcare system in Pakistan. There is no effective government healthcare credentialing system, no evidence-based recommendations for public health practices, and no regulation of rigorous regulations for public health, the inappropriate use of pharmaceuticals, patient safety, and the responsibility of healthcare professionals and organizations. In Pakistan, there are no standardized guidelines or instruments that clarify what constitutes proper clinical practice or research on the public health system. Public health boards and other local government entities in Pakistan have taken dramatic measures to encourage a culture of public health, get medical doctors involved in research, and build evidence-based clinical processess.

We learned that cognitive impairment based on hypertension can be prevented and treated if you know how the different risk factors work together, especially how a person's genes affect their risk. Those who have heart disease or high blood pressure are more likely to get aortic arch calcification. Also, most of the risk factors for developing hypertension are also risk factors for developing cognitive impairment based hypertension. Some of these risk factors are getting older, getting sick, being stressed out, and smoking. More research needs to be done to find out the direct and indirect validating assumptions that link important denominators with high blood pressure. This will make it possible to prioritize medical care for people with high blood pressure who live in Pakistan. This is an important step toward achieving the goal and will help Pakistan get closer to its goal. The research also shows that the evidence we have right now isn't very good, especially when it comes to hypertension and, more generally, the research and policy on the healthcare system in Pakistan as a whole.

Conclusions and Implications

According to the findings of this research :

1. A number of socio-demographic, pathophysiological, risk factors strongly correlate with hypertension.

2. To avoid and cure age-related cognitive impairment (also known as ARCI), it is critical to comprehend the interconnected risk factors, especially how a person's genetic composition impacts their risk.

3. Those with cardiac disease or hypertension are more likely to acquire aortic arch calcification.

4. Furthermore, the bulk of the risk factors associated with the onset of hypertension are also associated with the development of ARCI.

5. These risk factors include aging, illness, worry, and smoking. These associations might go either advantageously or adversely.

6. More research is required to study the direct and indirect causal inferences.

7. There are no established standards in Pakistan for what constitutes appropriate clinical practise or research on the public health system.

8. In Pakistan, public health boards and other local governmental bodies have taken significant steps to promote a culture of public health, involve clinicians in research, and develop evidence-based clinical procedures.

9. Some key denominators with hypertension bases studies are needed, so that Pakistani hypertensive patients can be given priority for medical care.

10. This would allow Pakistan to concentrate medical treatment for hypertensive patients.

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Declaration of interest: No conflict of interest is declared by authors.

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Tactics of managing children-patients with post-coagulopathy cardiac surgery interventions

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Abstract

Background: Children with congenital heart disease undergoing complicated pediatric cardiac surgery with cardiopulmonary bypass (CPB) experience considerable post-operative mortality and morbidity due to post-operative bleeding. An impairment in the blood clotting system primarily contributes to excessive bleeding in children following heart surgery.

Aim: to assess the different methods for the treatment of pediatric patients with post-coagulopathy cardiac surgery.

Methods: Pubmed, Web of Science, Scopus, Embase, SpringerLink, and the Cochrane Library in order to find various articles concerning this topic were searched. The search strategy; (cardiac surgery) AND (pediatric) AND (coagulopathy) AND (post-operative) was used. The investigation ended in April 2022.

Scientific novelty: Post-coagulopathy cardiac surgery is a relatively new medical field that has seen tremendous advances in the past decade. It involves the use of specialised techniques to reduce the risk of bleeding during and after cardiac surgery. This includes the use of anticoagulants, thrombolytics, and other medications to reduce clotting and improve outcomes. In addition, newer technologies such as robotic-assisted surgery have been developed to improve precision and accuracy during cardiac procedures. Therefore, this review aims to address the tactics of managing children-patients with post-coagulopathy cardiac surgery

Conclusion: The management of children-patients with post-coagulopathy cardiac surgery is a particularly challenging area due to their unique physiology and anatomy. As such, there is a need for novel approaches to ensure optimal outcomes for these patients. For example, research has shown that using anticoagulants in combination with thrombolytics can reduce the risk of bleeding complications following cardiac surgery in pediatric patients.

Keywords: cardiac surgery, pediatric, coagulopathy, post-operative, managemer

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Introduction

Haemostasis is the process of preventing and controlling bleeding; it is critical to maintain blood within a damaged blood vessel. A normal haemostatic systems include four components: vasculature, fibrinolytic proteins, coagulation factors, and platelets [1]. A deficiency in these components can cause coagulopathy. There are two types of coagulopathy: primary and secondary. A blood vessel or platelet deficiency is a primary

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haemostasis disease. Secondary diseases, on the other hand, involve quantitative or qualitative abnormalities in clotting factors or their inhibitors [2]. Children's cardiac surgery is a complicated and sensitive procedure that needs special care and knowledge. A number of heart diseases, including congenital heart defects, acquired heart disease, and other cardiac abnormalities, can be treated with the help of surgery. Paediatric cardiac surgery aims to improve the patient's quality of life by addressing the underlying issue and re-establishing normal heart function. The patient's and their family's management must be carefully considered during the delicate and complicated post-coagulopathy heart surgery. After post-coagulopathy cardiac surgery, educating young patients thoroughly about their condition is the first step in handling them. Medical personnel must clarify both the procedure's hazards and any potential consequences that can emerge. It's crucial to explain patients how to manage their food and lifestyle following the procedure as well as to explain the intake of needed medications. Cardiovascular illnesses are the leading cause of death worldwide, and during the past 20 years, the number of deaths from cardiac causes has rapidly increased. According to statistics, 7.3 million people die from cardiovascular diseases each year; by 2030, this number is predicted to rise to 23.6 million [3]. The number of cardiac procedures has significantly increased due to the rise in the prevalence of cardiovascular diseases. More than a million people worldwide have these kinds of operations every year. The increase in heart surgery rates supports the need to understand possible complications, such as bleeding, significantly contributing to mortality and morbidity [4].

Research Problem

Children that undergo complicated heart procedures often experience a variety of complications. One of the frequent and dangerous consequences of these operations is the post-operative coagulopathy. Physicians are unable to establish how to avoid such complications. Additionally, physicians find difficulties in determining how to manage the post-operative coagulopathy

Research Focus

In this review, one focused on determining the pathophysiology of coagulopathy after paediatric cardiac surgery and evaluating various ways to manage the coagulopathy that happen after cardiac operations in paediatric patients.

Research Aim and Research Questions

In this review, different methods for the treatment of paediatric patients with post-coagulopathy cardiac surgery are assessed.

1. What are the indications for paediatric cardiac surgery?
2. What are the causes of coagulopathy that happen after cardiac operations in paediatric patients?
3. What is the pathophysiology of coagulopathy after cardiac operations in paediatric patients?
4. What is the best way to manage coagulopathy and bleeding after cardiac operations in paediatric patients?

Research Methodology

General Background

Significant perioperative blood loss following paediatric cardiac surgery necessitates blood product transfusions. Transfusions in this susceptible population come with significant hazards and effects on clinical outcomes. The immaturity of the haemostatic system, excessive activation of the haemostatic system, hemodilution from the CPB circuit, and preoperative anticoagulant medications are some of the greater transfusion requirement causes in children. Clinicians use a variety of therapies to control bleeding because the causes of coagulopathy are frequently multifactorial. These therapies include antifibrinolytics to prevent fibrinolysis, cryoprecipitate or fibrinogen concentrate on raising fibrinogen concentrations, platelet transfusions to treat thrombocytopenia and platelet dysfunction, frozen plasma or prothrombin complex concentrate (PCC) to replenish depleted clotting factors and to enhance thrombin generation.

The first step in treating coagulopathy is identifying it; various patient and procedural risk factors have been found to be indicators of excessive bleeding. Pre-procedure medication management is essential since heart surgery patients frequently use anticoagulants or antiplatelet medications. Antifibrinolytics are crucial adjuncts to prevent transfusions, and there is conflicting evidence to support the use of perfusion techniques, including

sequestration, red cell salvage, and retrograde autologous priming of the bypass circuit. Detecting the patient's coagulation state enables targeted product replacement and reduces the need for transfusions of greater volume.

The aim of the work was to evaluate different tactics for managing children patients with post-coagulopathy cardiac surgery. PubMed, Web of Science, Scopus, Embase, SpringerLink, and the Cochrane Library were searched in order to find various articles concerning this topic. The next search strategy was used: (cardiac surgery) AND (pediatric) AND (coagulopathy) AND (postoperative) and the researches ended in April 2022. Some types of publications, such as proposals, letters, procedures, and opinions were excluded. The references involve articles that were chosen because of their relation to the topic.

Data Analysis

In this review, the results of previous trials and retrospective studies that tried to determine the best options for the management of coagulopathy after paediatric cardiac surgeries were gathered and compared. Any statistical analysis methods were not used the conclusions are made by comparing these results.

Research Results | Literature review

The title and the abstract were done, and then a full-text screening of these articles was accomplished in order to choose the articles related to our topic. Only a small number of the 486 papers concerned tactics for managing children patients with post-coagulopathy cardiac surgery interventions. Data on the coagulopathy rate after cardiac surgery in children and the management of this coagulopathy are adequately covered in 45 articles. Although they do not provide sufficient data for the aetiology of postoperative coagulopathy in children, they provide helpful information on the outcomes of different interventions for paediatric patients with postoperative coagulopathy in Figure 1.

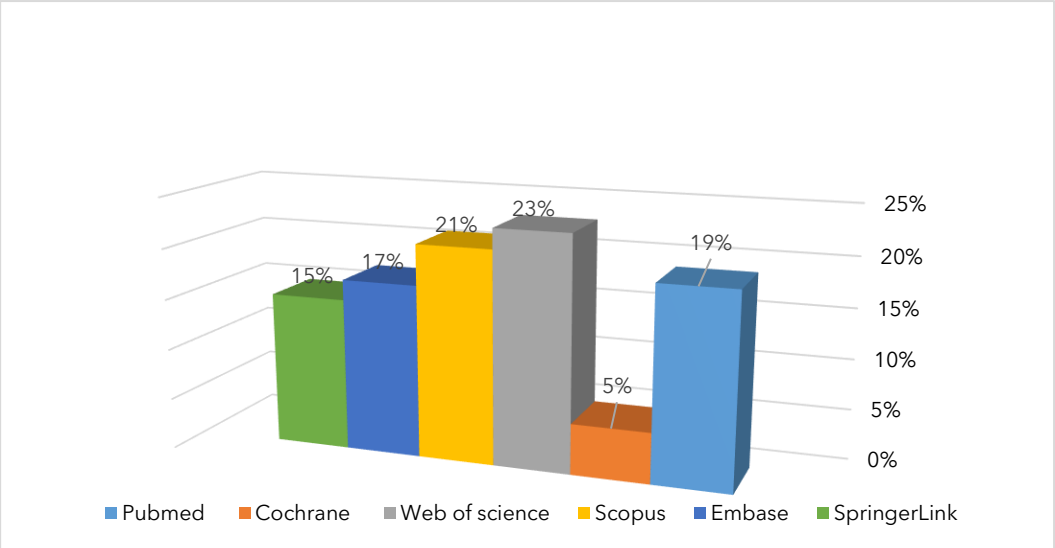

Figure 1. The results of our search

There are two types of coagulopathy: primary and secondary. A platelet or blood vessel abnormality is a primary haemostasis disease. In contrast, secondary diseases are characterised by quantitative or qualitative changes in the clotting factors or their inhibitors. Anticoagulants, inhibitors of certain factors, direct thrombin inhibitors, and non-specific inhibitors are all examples of inhibitors [5]. Most chronic disorders, including vitamin K deficiency, liver disease, anticoagulant therapy, and disseminated intravascular coagulation (DIC), are associated with acquired coagulation disorder [8, 9]. A deficiency in platelet number, factor deficiency, and the presence of circulating coagulation factor inhibitors are investigated using laboratory tests such as the complete blood count (CBC), prothrombin time (PT), activated partial thromboplastin time (aPTT), and mixing test in order to evaluate these disorders [6,7].

Perioperative coagulopathy is frequently observed in patients having heart surgery, and it is linked to significant bleeding, a higher need for blood transfusions, and repeated attempts to achieve surgical haemostasis. Postoperative morbidity, mortality, and expenses will all be negatively impacted by all of these

factors. Anticoagulants, antiplatelet medications, and genetic bleeding abnormalities are a few examples of preoperative causes of coagulopathy. Intraoperative variables are another cause of coagulopathy (e.g. hemodilution, consumption, and activation of coagulation factors and platelets, hypothermia, heparin administration, metabolic acidosis, hypocalcaemia, and excessive fibrinolysis). For the perioperative care of coagulopathy, preventative and therapeutic strategies are advised. There is conflicting information regarding the ability of preoperative or intraoperative testing to identify patients likely to experience severe bleeding after cardiac surgery due to coagulopathy. Preoperative evaluations of coagulation status, coagulation-interacting medications, and intraoperative coagulopathy risk factors constitute this preventive strategy's first step. During cardiovascular surgery, platelet dysfunction is a primary cause of bleeding, especially in patients on antiplatelet medications. Although platelet function assays are accessible, their use in assessing actively bleeding patients has not yet been proven. We consider appropriate Heparin antagonism, consistent clot stability/firmness by antifibrinolytics and blood products, and then platelet dysfunction in a sequential manner when dealing with surgical coagulopathy.

Pathophysiology of coagulopathy

Coagulation cascade

A perioperative clinician must recognise the complex relationships between the two systems that work together to keep the blood in circulation in a fluid state, especially when there is a pre-existing haematological problem. The haemostatic system is activated by pathological circumstances necessitating anaesthesia, surgery, or any other intrusive procedure. Trauma, pathogenic agents, or cytokines can also disrupt this balance. Thus, prothrombotic and prohaemorrhagic abnormalities are both highly likely to occur during the perioperative time [8]. Other factors that could make things worse include metabolic acidosis, extracorporeal circulation, hypoxia, and hypothermia.

The interactions between vessel walls, platelets, and adhesive proteins that result in the creation of the initial "platelet plug" are the cause of primary haemostasis. Numerous factors, including negatively charged heparin-like glycosaminoglycan, the synthesis, and secretion of platelet inhibitors, neutral phospholipids, coagulation inhibitors, and fibrinolysis activators, contribute to the antithrombotic properties of the endothelial cells lining the vascular wall. In comparison, the sub endothelial layer is quite thrombogenic and contains proteins, including laminin, vitronectin, and thrombospondin, that are important for platelet adherence in addition to von Willebrand factor (vWF) and collagen [9,10]. Arteriolar vasospasm, caused by any vascular injury, is mediated by neurogenic reflex mechanisms and the release of regional mediators such as platelet-derived thromboxane A2 (TxA2) and endothelin.

Coagulation cascade

Traditional classifications include extrinsic and intrinsic pathways, both leading to the activation of factor X. The traditional theory of blood coagulation is particularly helpful for comprehending in vitro testing, but it leaves out the crucial part played by cell-based surfaces in in-vivo coagulation. The following observations, however, do not seem to support contact activation, which is essential for in vivo haemostasis [11,12]. FXII, high-molecular-weight kininogen, or prekallikrein deficient individuals do not bleed excessively. In addition, individuals with hemophilia C, who are fully deficient in factor XI, experience mild haemorrhagic disease. Patients with only trace amounts of factor XI can survive substantial injuries without experiencing extraordinary bleeding [13,14]. Haemophilia A and B are caused by deficiencies of FIX and FVIII (intrinsic pathway factors); however, the traditional definition of two coagulation pathways leaves it unclear why either kind of hemophiliac cannot simply clot blood through the unaffected pathway Figure 2.

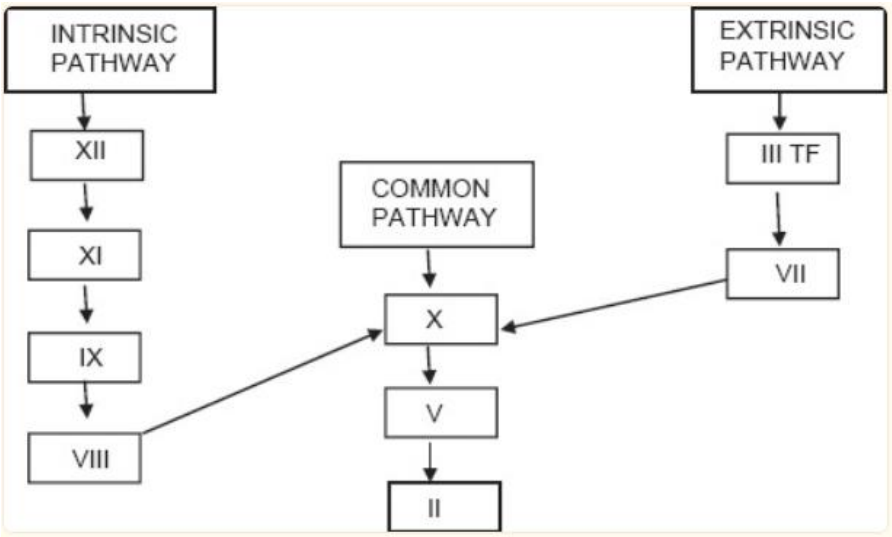

Figure 1. **Pathways of the coagulation process [15].**

Causes of coagulopathy

Coagulation disorders affect the body's capacity to regulate blood clotting. A thrombosis or haemorrhage might be the outcome of coagulation problems. There are various diseases that might lead to these clotting disorders [16]. Haemophilia**,** Von Willebrand disease, Liver Disease, DIC, Vitamin K deficiency, Platelet dysfunction, Factor V Leiden, Antithrombin III (ATIII) deficiency, Protein S or protein C deficiency, and Antiphospholipid antibody syndrome are disorders that cause coagulopathy [17]. Coagulopathy may be brought on by physiologic abnormalities like hypothermia, acidosis, or hemodilution brought on by the administration of fluid or blood. Still, it is also possible for severely injured patients to develop an acute coagulopathy independently of, or in addition to, these conditions [13,18,19]. This latter condition is referred to by several names in the literature, including the acute coagulopathy of trauma-shock (ACoTS), trauma-induced coagulopathy (TIC), early coagulopathy of trauma (ECT), and acute traumatic coagulopathy (ATC).

After paediatric heart surgery, coagulopathy is a frequent complication. This is mostly caused by hemodilution, which leads to platelet dysfunction and clotting factor depletion. It has been established that there is a direct correlation between blood loss, post-cardiopulmonary bypass (CPB) coagulopathy, and the need for transfusions. The morbidity and death rates following cardiac surgery increase when excessive bleeding occurs. The bleeding may be the result of surgical complications or poor haemostasis [20,21]. Cardiopulmonary bypass (CPB)-assisted cardiac surgery results in a coagulopathy that, in the event of a severe case, may increase the risk of perioperative bleeding complications. Early detection and characterization of coagulopathy increase the chance of starting countermeasures to reduce perioperative transfusion requirements and blood loss [22,23]. Thromboelastometry / thromboelastography (TEM/TEG) can detect perioperative coagulopathy, and routine intraoperative TEM/TEG has been shown to minimise transfusion requirements in both adult and paediatric cardiac surgery. The risk of bleeding complications in paediatric cardiac surgery is exacerbated by complex operations in low-weight children with an undeveloped coagulation system. Early detection and characterisation of the coagulopathy using TEM/TEG will maximise the chance for early treatment of haemostatic abnormalities if bleeding occurs [24,25]. Paediatric cardiac surgery research using TEM/TEG revealed that patients with congenital heart disease have defective clot formation, especially in children with cyanotic heart disease.

Aetiologies of cardiac surgery in children

In some cases, the surgery is life-saving and can help improving the life quality for a child. However, it is important to understand the potential causes of cardiac surgery in children so parents and caregivers can be aware of any potential issues. Congenital Heart Defects; One of the most common causes of cardiac surgery in children is congenital heart defects. These are structural problems with the heart that are present at birth. They can range from mild to severe and may require surgical intervention to correct them. Common congenital heart defects include ventricular septal defect (VSD), atrial septal defect (ASD), patent ductus arteriosus (PDA), tetralogy of Fallot, transposition of the great arteries, and coarctation of the aorta [26,27]. Paediatric cardiac surgery is a

specialised field of medicine that focuses on treating children with congenital heart defects. This type of surgery is typically performed by paediatric cardiologists and cardiac surgeons specially trained to treat children's hearts [28]. During the procedure, the surgeon will make an incision in the chest wall and use specialized tools to repair or replace damaged structures. Depending on the severity of the defect, this may involve repairing or replacing valves, arteries, veins, or other parts of the heart. Paediatric cardiac surgery aims to improve a child's quality of life by correcting any structural abnormalities that may be causing symptoms such as shortness of breath, chest pain, fatigue, and irregular heartbeat. In some cases, it can even save a child's life if left untreated. After surgery, children typically need to stay in the hospital for several days for monitoring and recovery before they can go home [29].

Acquired Heart Disease

Acquired heart disease refers to any condition that affects the heart after birth. It can be caused by infection, inflammation, or other medical conditions such as diabetes or high blood pressure. Some acquired heart diseases may require surgical intervention, such as valve repair or replacement or coronary artery bypass grafting (CABG) [30]. Early diagnosis and treatment can help improving outcomes for children with cardiac conditions and reduce their risk for complications from surgery.

Cardiac surgery intervention in children

Cardiac surgery intervention in children is a complex and delicate process that requires specialized care and expertise. It is a procedure that can be used to treat a variety of heart conditions, including congenital heart defects, acquired heart disease, and other cardiac abnormalities. The goal of cardiac surgery intervention in children is to improve the quality of life for the patient by correcting the underlying problem and restoring normal cardiac function [31,32].

Kazakhstan is home to a growing number of paediatric cardiac surgery centres, offering specialised care for children with congenital heart defects. These centres provide a range of services, from diagnosis and treatment to post-operative care. The country has seen a significant increase in the number of paediatric cardiac surgeries performed in recent years, with many of these procedures being performed on children from other countries in the region. The success rate for these surgeries is high, and the quality of care provided is excellent. With the help of highly trained medical professionals and state-of-the-art equipment, Kazakhstan is becoming an increasingly popular destination for paediatric cardiac surgery [28].

The first step in any cardiac surgery intervention in children is to diagnose the condition. This typically involves a physical exam, imaging tests such as an echocardiogram or MRI, and blood tests. Once the diagnosis has been made, the doctor will discuss with the family what type of surgery is best suited for their child's condition. Depending on the severity of the condition, it may be necessary to perform open-heart surgery or minimally invasive procedures such as catheterization or stenting [33].

The open-heart surgery is a major procedure that requires general anaesthesia and involves making an incision in the chest wall to access the heart. During this procedure, surgeons may repair or replace damaged valves or vessels, correct congenital defects, or perform bypass grafts to improve the blood flow to certain areas of the heart. Minimally invasive procedures are less invasive than open-heart surgery and involve inserting catheters into small incisions to repair or replace valves or vessels without incision in the chest wall [34]. After any type of cardiac surgery intervention in children, there will be a period of recovery time during which doctors will monitor their patient's progress closely. During this time, it is important for parents to follow all instructions given by their doctor regarding medications and activity levels for their child. In some cases, physical therapy may also be recommended to help strengthen muscles weakened by prolonged bed rest during recovery from open-heart surgery.

Overall, cardiac surgery intervention in children can be a life-saving procedure when correctly performed by experienced medical professionals. It can help restore normal cardiac function and improve the quality of life for patients with serious heart conditions.

Management children-patients with post-coagulopathy

Post-coagulopathy cardiac surgery is a complex and delicate procedure that requires careful management of both the patient and their family. This article evaluates some tactics for managing children-patients with post-coagulopathy cardiac surgery.

The first step in managing children-patients with post-coagulopathy cardiac surgery is to provide them with comprehensive education about their condition. It is important for healthcare professionals to explain the risks associated with the procedure, as well as any potential complications that may arise. Additionally, it is important

to provide information about how to manage their diet and lifestyle after the procedure, as well as any medications they may need to take. This education should be personalized to each individual patient's needs and should be provided in a way that is easy for them to understand [35]. It is also important for healthcare professionals to provide emotional support for children-patients with post-coagulopathy cardiac surgery. This can include offering reassurance, listening to their concerns, and providing comfort during difficult times. Additionally, it can be beneficial for healthcare professionals to involve family members in the care process so that they can provide additional support and understanding. It is also important for healthcare professionals to monitor the progress of children-patients with post-coagulopathy cardiac surgery closely. This includes regularly assessing their physical condition, monitoring vital signs, and performing any necessary tests or procedures as needed. Additionally, it is important for healthcare professionals to keep track of any changes in symptoms or behaviour so that they can intervene if necessary.

Several studies have indicated that providing antifibrinolytic drugs after paediatric-cardiac surgery lowers the activation of the inflammatory and fibrinolytic systems, based on our understanding of the pathophysiology of post-cardiac surgery coagulopathy. It also reduces postoperative blood loss and the requirement for blood transfusions. Tranexamic acid, aprotinin, and aminocaproic acid are examples of pharmaceutical agents [37, 38]. Thrombolytic drugs work by causing fibrin, von Willebrand factor, and platelet surface glycoproteins (GPIb and GPIIb/IIIa) to degrade. A similar activity was observed during and after conducted cardiopulmonary bypass (CPB), which resulted in platelet dysfunction. As a result, the fibrinolytic-induced platelet deficiency may be decreased by using antifibrinolytic medications such aprotinin, which inhibit fibrinolytic enzyme activity. (38). Patients receiving aprotinin therapy for CPB had normal 2-antiplasmin levels, preserved GP1b platelet receptors, better platelet aggregation, and less blood loss than patients who do not get aprotinin medication. Other antifibrinolytic drugs, such as tranexamic acid and aminocaproic acid, have similar effects; however they are less effective against platelet dysfunction and receptor lysis than aprotinin.

Finally, it is essential for healthcare professionals to ensure that children-patients with post-coagulopathy cardiac surgery receive follow up care after the procedure has been completed. This includes regular appointments with a cardiologist or other specialist as well as ongoing monitoring of their condition by primary care providers or other medical personnel. Additionally, it can be beneficial for patients and families to receive counselling or other forms of psychological support if needed in order to help them cope with any emotional issues related to their condition or treatment plan [39]. By following these tactics, healthcare professionals can ensure that children-patients with post-coagulopathy cardiac surgery receive comprehensive care throughout every stage of their treatment plan. By providing education about their condition, offering emotional support, monitoring progress closely, and ensuring follow up care after the procedure has been completed, healthcare providers can help ensure positive outcomes for these patients and their families. Table 1 one compares the fresh frozen plasma and recombinant factor concentrates.

Table 1. Compares the fresh frozen plasma and recombinant factor concentrates

Criteria	Fresh Frozen Plasma	Recombinant Factor Concentrates
Source	Donated human blood	Produced through genetic engineering
Composition	Contains all clotting factors and plasma proteins	Contains specific clotting factors
Administration	Requires blood typing and cross-matching, takes time to thaw and prepare for use, requires large volume infusion	Can be administered quickly, does not require blood typing or cross-matching, smaller volume infusion
Efficacy	Can correct coagulopathy in most cases, but may not provide enough of specific clotting factors in severe cases	Provides specific clotting factors needed for correction of coagulopathy, more effective in severe cases
Risks/Complications	Risk of transfusion reactions, transmission of infections, fluid overload, allergic reactions, and transfusion-related acute lung injury (TRALI)	Risk of allergic reactions and inhibitors formation
Cost	Relatively inexpensive compared to factor concentrates	More expensive than fresh frozen plasma

Discussion

The likelihood of post- CPB bleeding has been predicted by a number of patient and procedural risk factors. Older age, body habitus, critical preoperative status, impaired renal and hepatic function, prior cardiac surgery, surgical complexity, ventricular assist device implantation or explantation, heart transplantation, and most importantly, the length of CPB, are non-modifiable risk factors [40,41]. Short cessation times for antiplatelet medications and other anticoagulants, preoperative anaemia and thrombocytopenia, and nadir CPB haemoglobin levels are all modifiable risk factors for perioperative coagulopathy [42].

Sebastian et al [43] found that transfusion of blood components is frequently required due to the nature and complexity of heart surgery. However, there is growing evidence that it is not benign and may result in harmful effects following cardiac surgery. Fresh whole blood (less than 48 hours from donor to transfusion) has been shown to minimise haemorrhage in children under the age of 2 who are having difficult congenital heart surgery [44]. However, other studies have not demonstrated any advantages of fresh whole blood. Antifibrinolytics are drugs that inhibit the breakdown of fibrin, a protein that forms blood clots. They are commonly used in the management of post-cardiac surgery coagulopathy to prevent excessive bleeding. The most commonly used antifibrinolytic drug in cardiac surgery is tranexamic acid (TXA). TXA has been shown to reduce blood loss and transfusion requirements in patients undergoing cardiac surgery. However, there are concerns about its potential side effects, such as thromboembolic events and renal dysfunction. Epsilonaminocaproic acid (EACA), tranexamic acid (TXA), and aprotinin, a serine protease inhibitor, are effective in lowering bleeding and transfusion in paediatric patients following heart surgery. Many centres switched to EACA or TXA when most institutions stopped carrying aprotinin. Every medicine has a different dosage regimen [45]. Recently, it has been reported that TXA dose regimens based on pharmacokinetic modelling and intended to create low, moderate, or high plasma concentrations in neonates and babies under 2 months of age, infants between 2 and 12 months of age, and children more than 12 months of age. Similar to the neonatal dose adjustment for EACA, these dosage recommendations account for age-related variations in clearance and are intended to create a specific concentration in the bypass prime rather than a weight-based bolus. Coagulation factor concentrates (CFCs) have been used in the management of post-cardiac surgery coagulopathy for several decades. Post-cardiac surgery coagulopathy is a common complication that occurs after cardiac surgery, and it is characterized by abnormal bleeding and clotting. The use of CFCs has been shown to be effective in managing this condition, and it has become an important part of the standard of care for patients undergoing cardiac surgery. CFCs are derived from human plasma and contain specific clotting factors that are deficient in patients with coagulopathy. These factors include factor VIII, factor IX, factor XIII, and von Willebrand factor. CFCs are available in different formulations, including fresh frozen plasma (FFP), cryoprecipitate, prothrombin complex concentrate (PCC), and recombinant factor concentrates [46]. FFP is the most commonly used CFC in the management of post-cardiac surgery coagulopathy. It contains all the clotting factors found in plasma and can be used to replace multiple clotting factors simultaneously. However, FFP has several limitations, including the need for blood typing and cross-matching, a high risk of transfusion-related complications such as transfusion reactions and infections, and a limited shelf life [47]. Cryoprecipitate is another form of CFC that contains high concentrations of fibrinogen, von Willebrand factor, and factor VIII. It is often used as an alternative to FFP when fibrinogen levels are low or when there is a need for rapid correction of bleeding. PCC is a concentrated form of clotting factors II, VII, IX, and X that can be used to rapidly correct coagulopathy. PCC has several advantages over FFP, including a lower volume requirement for administration, a longer shelf life, and a lower risk of transfusion-related complications. Recombinant factor concentrates are synthetic forms of clotting factors that are produced using genetic engineering techniques [48]. They have several advantages over plasma-derived CFCs, including a lower risk of viral transmission and a longer shelf life. However, they are more expensive than plasma-derived CFCs and may not be readily available in all healthcare settings. The use of CFCs in the management of post-cardiac surgery coagulopathy is based on the principle of replacing deficient clotting factors to restore normal haemostasis. The choice of CFC depends on the specific clotting factor deficiency, the severity of coagulopathy, and the patient's clinical condition. Several studies have demonstrated the effectiveness of CFCs in managing post-cardiac surgery coagulopathy. A randomised controlled trial conducted by Pei et al. showed that the use of PCC was associated with a significant reduction in bleeding and transfusion requirements compared to FFP in patients undergoing cardiac surgery [48]. Another study by Despotis et al. showed that the use of cryoprecipitate was associated with a significant reduction in bleeding and transfusion requirements compared to FFP in patients undergoing coronary artery bypass grafting [49].

Kunz et al [41] performed a single-centre, retrospective study and found that a higher protamine: heparin ratio may be associated with adverse haemostatic effects, with lower ratios associated with a 10 g/L lower haemoglobin differential on arrival to the ICU, a 70 ml lower drain tube output at 4 hours, and a 56% reduction in red cell

transfusion. Given the high morbidity and mortality associated with post-operative anaemia and transfusion, this provides another possible haemo conservation technique.

Bartoszko et al [50] found that platelet dysfunction, hypofibrinogenemia, reduced thrombin production, and hyperfibrinolysis are the four most critical underlying processes for coagulopathy in this setting. In terms of the inflammatory component of coagulopathy, there is no evidence that immunologic or anti-inflammatory therapies are successful in changing patient outcomes.

Despite their effectiveness, the use of CFCs in the management of post-cardiac surgery coagulopathy is not without risks. The most common adverse events associated with CFC administration include thromboembolic events, allergic reactions, and transfusion-related complications.

Conclusions and Implications

1. It is important providing a safe and supportive environment for children-patients with post-coagulopathy cardiac surgery.

2. Parents should be involved in the care of their children-patients in order to ensure and to receivie the best possible care.

3. Procedural risk factors for postoperative coagulopathy include: older age, body habitus, critical preoperative status, impaired renal and hepatic function, and prior cardiac surgery.

4. A close monitoring of vital signs and laboratory values should be conducted to ensure the proper patient's recovering.

5. Additional information about post-operative care and lifestyle modifications should be provided to both the patient and their family members to ensure a proper recovery and long-term health outcomes.

7. Regular appointments should be scheduled in order to monitor the progress and to address any concerns or issues that may arise during recovery.

8. Fresh frozen plasma and recombinant factor concentrates are both effective in managing post cardiac surgery coagulopathy in children.

9. The choice between fresh frozen plasma and recombinant factor concentrates should be based on the specific patient needs, including their age, weight, and medical history.

10. Recombinant factor concentrates are more targeted and have a lower risk of adverse reactions, but they may be more expensive and less readily available than fresh frozen plasma.

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Ukrainian paediatrics of the future: current problems and prospects for improvement

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Abstract

This article focuses on "Ukrainian paediatrics of the future: current problems and prospects for improvement.

Aims: objectives of the research study are to identify the current problems and challenges facing paediatric healthcare in Ukraine, including issues related to healthcare professionals, infrastructure, vaccination coverage, healthcare spending and public awareness of paediatric health and prevention; areas for improvement after analyses of previous initiatives; potential for future improvements in paediatric healthcare in Ukraine, including prospects related to national vaccination programs, telemedicine and digital health, medical research, the patient-centered care, medical education and training, improved healthcare infrastructure, and public-private partnerships.

Study design: Descriptive cross-sectional study

Place and Duration of Study: The majority of the studies were conducted on patients, professionals' healthcare establishment and policy maker stakeholders in the Ukraine.

Methodology: In order to collect secondary data a questionnaire was used.

Results: Ukraine has just 665 hospital beds per 100,000 residents in 2019 compared to 417 doctors per 100,000 in 2000. The pace of replacement for most medical equipment is sluggish. Since 2019, the rates of infant, under-five, and neonatal death have been mostly steady. The rates of BCG and measles vaccination coverage have fluctuated, although they have typically gone down. The biggest problem with paediatric healthcare in Ukraine is a lack of money, which leads to a dearth of medical personnel, supplies, and equipment, as well as a high incidence of diseases that may be prevented because of a lack of public awareness of paediatric health.

Conclusion: Paediatrics faces challenges, including inadequate healthcare infrastructure and a high infant and child mortality rate. Prospects for improvement, such as the development of telemedicine and e-health services, improving maternal and child healthcare services, and increasing investment in research and development. By addressing these challenges and investing in these prospects, the country can significantly improve the health and wellbeing of its children.

Keywords: Ukrainian; paediatrics; current problems; prospects; future; improvement.

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Introduction

The Ukrainian People's Republic was recognized in 1917. Following its engagement, the Soviet Union ruled the Ukrainian SSR for almost 70 years. The Ukrainian SSR expanded westward when Nazi Germany and the USSR invaded Poland in 1939. In 1954, it extended southward with the Crimea. Ukraine obtained independence in 1991 as the Soviet Union fell. Ukraine's market economy transition has caused a socioeconomic disaster for over 20 years [1].

Paediatrics is vital since it treats babies, children, and adolescents. Ukraine, like many other countries, must overcome a lack of funding, resources, medical equipment, and staff training to deliver efficient paediatric care. These issues are exacerbated by the nation's political and economic instability. Paediatricians and family physicians treat 50% of Ukraine's youngsters. Family and paediatricians treat children from birth to 18 years. A doctor sees 800 people every year [2].

The literature published between 2018 and 2021, emphasising the most recent advances in the discipline. The difficulties paediatric healthcare in Ukraine faces are caused by a number of variables. The high infant mortality rate, which is 6.5 deaths for every 1,000 live births, is an issue. In 2021, the mortality rate for infants in Ukraine was among the lowest in the world at 7 fatalities per 1,000 live births. Only 1.6 paediatricians are available for every 1,000 children in the nation, indicating a dearth of paediatric medical specialists. Other factors aggravating the issue include underfunding of the healthcare system, out-of-date medical technology, and a scarcity of critical pharmaceuticals [3].

The quality of primary medical care provided to mothers and babies, access to such services, especially for socially vulnerable groups and the rural population. The absence of national standards for child development, the lack of adequate access to a children's hotline that provides information, psychological, and legal assistance to children, and the number of registered internally displaced children reaching 215 are among the other current issues in paediatric health. This year, there have been at least 36 verified attacks on schools in communities situated within 15 kilometres of the contact line in combat zones. More than 400,000 children need ongoing support to cope with the psychological wounds left by growing up in the midst of a long fight [4]. In order to ensure both the mother's and the child's health and wellbeing, both must have access to primary medical care and for the purpose of lowering health inequalities and advancing fairness, it's crucial to provide socially disadvantaged populations and the rural population access to basic medical care equally preventive and curative. The quality of the given care to children may be improved, and it can be made sure that they get the right care at each stage of their life development process by creating national standards for child development. The access to a children's hotline that offers advice, counselling, and legal support may help guarantee that kids have the resources they need to be safe and healthy. Ensuring that internally displaced children get the attention and assistance they need during a difficult and stressful period is essential the difficulty of rising a universal approach to child development, which may not take into account individual characteristics and requirements, may be the cause of the lack of national standards for child development. The internally displaced children who have registered may not fully represent the entire number of internally displaced children since other families may choose not to do so out of mistrust or fear of the government. Attacks on schools in war areas are a larger problem connected to security and conflict that may go beyond the purview of paediatric health alone. Although it's crucial to continue supporting kids who are dealing with psychological wounds, doing so could not address the underlying reasons for the war and displacement that caused those wounds in the first place. All these issues are major concern associated with low quality paediatrics healthcare services.

In Ukraine, paediatricians care for the other half of the youngsters while family physicians serve the other half. From birth to age 18, paediatricians and family physicians care for children. Contracts have been signed between the NHSU and more than 600 primary healthcare providers, including non-profits, for-profits, and physician entrepreneurs. Since 2018, all primary healthcare providers have met with all requirements, registered with the eHealth system, and signed an agreement with the NHSU. Beginning in 2019, people will receive full reimbursement for primary care services via an NHSU-funded contract-based age-adjusted capitation system. [5].

In Ukraine acute respiratory illnesses, diphtheria, measles, chickenpox, and cholera are prevalent infectious diseases. People in crisis may also be more susceptible to infectious diseases. Critical factors include the ability of governments or non-governmental organisations to sustain fundamental childhood immunisation programs and the speed at which disease outbreaks are identified and treated with drugs designed for that illness. Ukrainian paediatricians have the opportunity to thrive as a result of the national immunisation program, telemedicine and digital health, medical research, medical education and training, enhanced healthcare infrastructure, and public-private collaboration [6].

Additionally, a number of organisations seek to provide healthcare institutions with medical supplies and equipment as well as training for healthcare professionals [7]. To stop the spread of infectious illnesses, it is crucial for governments and non-governmental organisations to maintain children vaccination programs and provide digital health to the people who live in rural places or who are unable to leave their houses due to a crisis scenario. Improved alternatives for infectious disease prevention and treatment may result from medical research and education. Healthcare reforms may be funded and carried out with the aid of public-private partnerships. The quality of patient care in Ukraine may be enhanced by providing medical supplies and training for healthcare workers. Keeping in view the current frequency of infectious illnesses there, it is possible that present efforts at prevention and treatment are insufficient. Budget restrictions or political instability may make it difficult for governments and non-governmental groups to maintain vaccination programs. All Ukrainians may not have access to telemedicine and digital health, especially those who live in poverty or don't have stable internet connectivity. In times of crisis, medical research and education may not get enough money or attention. Disputed interests or a lack of accountability may make it difficult for public and private sectors to work together. Analysing earlier studies on resources, healthcare workers, and public knowledge on paediatric health and prevention in Ukraine, investigating the results of earlier efforts to enhance paediatric care in Ukraine the funding, healthcare workers, inadequate infrastructure, political and economic instability, corruption in the health sector, and public awareness of paediatric health and prevention are just a few of the previously studied aspects of paediatric healthcare in Ukraine [8–10].

In conclusion, there are a number of issues with paediatric healthcare in Ukraine. However, there are a number of efforts targeted at improving the system, and with continuous funding and assistance, paediatric healthcare in Ukraine seems to have a bright future. Paediatric healthcare in Ukraine has a promising future despite its difficulties. Although infectious illnesses are still widespread, attempts are being done to combat them. The prevention of disease outbreaks depends on effective childhood vaccination programs. The remote or crisis-affected communities may have better access to healthcare thanks to telemedicine and digital health. Better preventive and treatment options may result from medical research and education. A more efficient healthcare delivery may be supported by improved healthcare infrastructure. Initiatives may get money and assistance for their execution thanks to public-private partnerships. The supply of medical equipment and training for medical staff members may enhance the standard of service. To maintain and advance upon accomplishments established, ongoing financing and help are required. Paediatric healthcare in Ukraine has the potential to significantly advance with continued efforts and assistance.

Research Problem

The research problem of the study on "Ukrainian paediatrics of the future: current problems and prospects for improvement" include such questions:

1. What are the causes of the lack of medical personnel in Ukraine's paediatric sector?
2. How is the quality of paediatric healthcare in Ukraine impacted by the lack of suitable infrastructure, medical equipment, and supplies?
3. What illnesses affect children the most often in Ukraine?
4. What factors contribute to Ukraine's low immunisation rates, and how may they be raised?
5. How paediatric healthcare are services available and of a high standard in Ukraine affected by the country's inadequate healthcare spending?

Research Focus

The goal of the research study "Ukrainian paediatrics of the future: current problems and prospects for improvement" is to examine potential strategies for enhancing the quality and accessibility of paediatric care in the future by analysing the state of paediatric healthcare in Ukraine today, identifying the biggest difficulties and issues the healthcare system is currently facing, and analysing the current situation.

Research Aim and Research Questions

The objectives of the research study are:

1. To identify and examine the existing concerns and difficulties related to healthcare professional in paediatric healthcare in Ukraine.
2. To identify and examine the existing concerns and difficulties related to healthcare infrastructure and equipment in paediatric healthcare in Ukraine.

3. To identify and examine the existing concerns and difficulties related to vaccination coverage in paediatric healthcare in Ukraine.

4. To identify and examine the existing concerns and difficulties related to mortality (BOD) in children in Ukraine.

5. To identify and examine the existing concerns and difficulties related to healthcare spending in paediatric healthcare in Ukraine.

Research Methodology

General Background

In Ukraine, the medical discipline of paediatrics is dedicated to the treatment of new-borns, kids, and teenagers. The Ukrainian paediatric healthcare system confronts several difficulties despite recent advancements in healthcare services. The healthcare system is suffering from a lack of funds and antiquated infrastructure as a result of the nation's economic and political disorder. This has led to a lack of paediatricians, especially in rural regions with underfunded and understaffed healthcare institutions.

There are a number of measures that may be used to enhance the condition of paediatrics in Ukraine. These include boosting healthcare financing, raising the standard of doctor training and education programs, and implementing all-encompassing preventative healthcare initiatives. The general public understanding of the value of routine check-ups, vaccinations, and good lifestyle practices may also be raised.

Paediatric healthcare in Ukraine has many difficulties overall, but there is also a lot of room for progress. The nation can offer all children with top-notch paediatric care and guarantee a healthy future for the next generation by putting the aforementioned plans into practice.

Sample / Participants / Group

The following sample/participants/groups was involved in the research "the future paediatrics healthcare sector in in Ukraine":

1. Healthcare workers.

2. Healthcare institutions.

3. Patients.

4. Key stakeholders (healthcare policymakers, healthcare professionals, and experts in digital healthcare solutions).

Instrument and Procedures

For the purpose of gathering data, a questionnaire was used. Using both online and offline techniques, secondary data was gathered for the questionnaire from official sources and public data. Data analysis techniques may use both quantitative and qualitative methodologies. The study results might be shown as a table or graph.

Data Analysis

A quantitative data analysis with the implementation of descriptive statistics, such as frequency tables, mean, median, mode, standard deviation, and range, in order to summarise and characterise the obtained information from surveys was used. There was no data analysis and just a data comparison in the discussion part.

Research Results

Statistical data for Ukraine

The statistics results (Table 1) for Ukraine include information on the country's population's age distribution, ethnic composition, level of education, health, and other characteristics. The population of Ukraine, excluding Crimea and Sevastopol, was 41,130,432 as of the most recent statistics. According to reports, the country's population growth rate was 6.6 new residents per 1,000 inhabitants. In contrast to the mortality rate of 14.7 per 1,000 people, there were 8.1 births per 1,000 people. In Ukraine, the average lifespan was 71.76 years, with men living to an average age of 66.69 years and females living to an average age of 76.72 years. According to the population of Ukraine's age breakdown, 15.4% of people were under the age of 14, 68.4% were between the ages of 15 and 64, and 16.2% were 65 years of age or over. According to reports, 1.16 children were born for

every woman in Ukraine in 2021. In 2015, there were 5.4 migrants per 1,000 persons, or the net migration rate. At birth, there were 1.06 more boys than females. The gender ratio for individuals under the age of 15 was 1.06 men to females. The sex ratio was 0.92 men for every female for those between the ages of 15 and 64, and 0.51 males for every female for those 65 and older [11].

Table 1. Demographic Characteristics

Variable	Frequency
Total population	41,130,432
Growth rate per 1000 population	6.6
Birth rate per 1000 population	8.1
Death rate per 1000 population	14.7
Life expectancy	71.76 years

Source: Authors' development based on state statistics service of Ukraine [14]

Status of Healthcare staff

The results according to a study conducted in Ukraine (Table 2) the number of doctors per 100,000 individuals, excluding dentists, decreased from 462 in 2000 to 417 in 2019. This suggests a decline in the availability of medical professionals in the country. The study also found that the number of nurses and midwives per 100,000 people in Ukraine decreased from 1103 in 2000 to 743 in 2019. This indicates a significant reduction in the number of healthcare professionals providing care to patients in the country. Moreover, the study reported that in 2019, there were 665 hospital beds per 100,000 individuals in Ukraine, down from 950 in 2000. This reduction in the number of hospital beds available per capita could potentially have an impact on the accessibility of medical care in the country [12].

Table 2. Status of healthcare professional in Ukraine Click or tap here to enter text.

Rates	2000	2019
Physicians per 100 000 population	462	417
Nurses and midwives per 100 000 population	1103	743
Number of hospital beds per 100 000 population	950	665

Source: Authors' development based on health systems in action: Ukraine [12]

The decline in the number of doctors and healthcare professionals in Ukraine indicates a potential lack of healthcare providers. The reduction in hospital beds per capita could lead to longer wait times and limited access to medical care. The decline in the number of nurses and midwives in Ukraine could lead to a shortage of caregivers, particularly for vulnerable populations. It is important to address the root causes of these reductions in order to improve access to healthcare in the country. Strategies such as increasing funding for medical education and expanding healthcare infrastructure may be needed to address these issues. The research does not take into consideration population fluctuations in Ukraine, which can have an impact on the number of physicians, nurses, and hospital beds per capita. The possible effects of technology and telemedicine on access to healthcare in Ukraine are not taken into account by the research. There may be a move toward greater outpatient treatment, as seen by the decrease in hospital beds per capita.

Status of Infrastructure, Equipment and Supplies

The results concerning the supply and maintenance of medical equipment in Ukraine's healthcare system showed that the majority of medical equipment in the country has been in use for 20 to 25 years, far beyond its recommended lifespan. Replacement rates for old and worn-out equipment have been slow, which has resulted in many hospitals and clinics operating with outdated and ineffective equipment. Furthermore, the COVID-19 pandemic has exacerbated the already existing problem of a shortage of hospital beds in Ukraine. The number of hospital beds available per 100,000 individuals decreased from 950 in 2000 to 665 in 2019. This decline of 665 hospital beds per 100,000 individuals has put additional pressure on the healthcare system during the pandemic. It has become increasingly difficult to accommodate the rising number of COVID-19 patients, resulting in long wait times and insufficient medical care for those in need [12].

Status of burden of disease

Results of the available statistics showed the infant mortality rate (Table 3) were 7.3, 7.1 and 7 in year 2019, 2020 and 2021 respectively. Fewer than 5 mortality rates were 8.5, 8.4 and 8.2 in years 2019, 2020 and 2021 respectively while neonatal mortality rates were 4, 98, 4.89 and 4.83 in years 2019, 2020 and 2021 respectively. The following list of unfavourable childhood experiences was experienced by at least two of the 20.8% of Ukrainian children: Parental passing, child welfare involvement, major sickness or injury, home drug or alcohol misuse, household mental illness, parental divorce or separation, physical or sexual abuse, a family member serving time in jail or becoming a criminal [13,14].

Table 3. Mortality rate from 2019 to 2021 in Ukraine

Variable	2019	2020	2021
IMR	7.3	7.1	7
Under5 mortality	8.5	8.4	8.2
Neonatal Mortality	4.98	4.89	4.83

Source: Authors' development based on UNICEF data [13,14]

Vaccination status

The results of the available statistics (Table 4) showed that the year 2021, 88.5% of individuals received the first dose of the measles-containing vaccine, while in 2020 and 2019; the coverage rates were 84.9% and 93.2%, respectively. Similarly, for the second dose of the measles-containing vaccine, the coverage rates were 85.9%, 81.9%, and 91.7% in 2021, 2020, and 2019, respectively. The BCG vaccine coverage rates were 86.5%, 92.7%, and 83.8% in 2021, 2020, and 2019, respectively. For the DTP-containing vaccine, the coverage rate for the first dose was 90.8%, 92.6%, and 88.9% in 2021, 2020, and 2019, respectively. However, for the third dose, the coverage rates were 78.1%, 81.3%, and 79.9% in 2021, 2020, and 2019, respectively. The coverage rate for the third dose of Hib vaccine was 87.2%, 85.2%, and 80% in 2021, 2020, and 2019, respectively. The Hepatitis B vaccine coverage rate at birth was 90.4% and 100% in 2021 and 2020, respectively. The coverage rate for the third dose of polio vaccine was 78.3%, 84.2%, and 77.8% in 2021, 2020, and 2019, respectively. For the first dose of rubella-containing vaccine, the coverage rates were 88.5%, 84.9%, and 93.2% in 2021, 2020, and 2019, respectively [15].

Table 4. Vaccinations Coverage from 2019 to 2021

Vaccination Name	2021	2020	2019
Measles-containing vaccine, 1st dose	88.5%	84.9%	93.2%
Measles-containing vaccine, 2nd dose	85.9%	81.9%	91.7%
BCG	86.5%	92.7%	83.8%
DTP-containing vaccine, 1st dose	90.8%	92.6%	88.9%
DTP-containing vaccine, 3rd dose	78.1%	81.3%	79.9%
Hib, 3rd dose	87.2%	85.2%	80%
HepB, 3rd dose	77%	80.9%	76.5%
HepB, birth dose (given within 24 hours of birth)	56.3%	68.6%	60.3%

HepB, birth dose total (including those given within and after 24 hours of birth)	90.4%	100%	
Flu for all persons above >6 months (universal recommendation)	0.27%		
Influenza child age group 1	0.68%	1.11%	40%
Influenza child age group 2			52%
Polio, 3rd dose	78.3%	84.2%	77.8%
Rubella-containing vaccine, 1st dose	88.5%	84.9%	93.2%

Source: Authors' development based on WHO Immunisation data portal [15]

The results of the available statistics (Table 5) showed that Ukraine has a higher infant mortality rate of 7% than neighbouring European nations like Belarus and Russia, which had infant mortality rates of 2% and 5%, respectively. The death rate for children under the age of five is 8% in Ukraine, 3% in Belarus, and 6% in Russia. In Russia, Belarus, and Ukraine, the death rate for children aged 5 to 14 is 2%, 1%, and 2%, respectively. In Russia, 6% of infants are born weighing less than 2500g, compared to 5% in Belarus and 6% in Ukraine

Table 5. Mortality Status in Ukraine and neighbouring countries, according to 2021 UNICEF report Click or tap here to enter text.

Vaccination Name	Ukraine	Belarus	Russia
Under–5 mortality (%)	8	3	6
Infant mortality (%)	7	2	5
Mortality rate, children 5–14 years (%)	2	1	2
Low birth weight <2500g (%)	6	5	6

Source: Authors' development based on UNICEF [30]

Status of Healthcare spending

The lack of sufficient finance is one of the main issues paediatric healthcare in Ukraine is experiencing. Due to this, there is a lack of healthcare workers as well as medical supplies and equipment. A high prevalence of avoidable children's diseases is also a result of a lack of public understanding about paediatric health and prevention [16]

The results from the data that is currently available show that domestic general health expenditure per capita, PPP (the current international $), domestic general government spending on health (% of current health expenditure), and external health spending per capita, PPP (current international $) in 2019 are 51.12, 54.53, and 248.13 respectively. PPP (current international dollars) domestic health care expenditure per person is 907.16 [17].

The Ukrainian paediatric healthcare system is afflicted by a lack of medical experts, antiquated equipment, and inadequate money. There are 41.1 million people, with a birth rate of 8.1 and a death rate of 14.7. Ukraine has a life expectancy of 71.76 years. Ukraine lost physicians and hospital beds per 100,000 people between 2000 and 2019, restricting medical services. Slow replacement rates have exacerbated the hospital bed shortage, which has decreased from 950 in 2000 to 665 in 2019 and has resulted in excessive wait times and inadequate medical care. In Ukraine, the infant mortality rate was 7.3, 7.1, and 7 per 1,000 live births in 2019–2021, respectively. The mortality rate for children under the age of five has remained high, with rates of 8.5, 8.4, and 8.2 per 1,000 children in 2019, 2020, and 2021, respectively. Ukraine's newborn and child mortality rates are greater than those of Belarus and Russia due to the above-mentioned causative factors. In Ukraine, vaccination coverage rates are very poor. The coverage rates for the first measles immunization dose, polio, and DTP third-dose coverage were very low. Hepatitis B birth immunisation has recently gained popularity in Ukraine. The Ukrainian paediatric healthcare system is very weak, medical expertise, equipment, and supplies are scarce due to underfunding, and children are at risk of avoidable infections. Foreign health spending per person is 248.13 PPP, whereas domestic general government health spending is 54.53 PPP and domestic general health spending is 51.12 PPP. Healthcare in the United States costs $907.16 PPP per person; this also shows very low budget spending on health. Finally, Ukraine's paediatric healthcare system is plagued by a lack of medical staff and equipment, inadequate funding, and high new-born and child death rates and requires a comprehensive strategy that tackles the underlying reasons while also funding appropriate medical experts, equipment, and supplies.

Discussion

Status of Healthcare staff

The paediatric healthcare system in Ukraine offers services via specialists in 50% of cases and regular physicians in 50% is suffering from a physician and nurse lack, particularly in rural regions. In recent years, there have been fewer doctors in Ukraine. The workforce is aging; as of 2019, 24.7% of active physicians were retired, which one reason is contributing to this trend. Additionally, there has been a rise in doctors looking for employment outside the public health system as well as in the emigration of healthcare professionals.

While when paediatric primary care is compared in other countries in Europe, variations exist among them, as shown by a study conducted in 29 countries. A family doctor or general practitioner system was used by 41% of them, a paediatrician-based system by 24%, and a combination system of healthcare services by 35%. There were 82 078 paediatricians in all of the 29 nations. 40.4% of these were employed in primary care. The issue of healthcare personnel lack in many nations is complex. The dearth of health professionals was mostly caused by elements like poor pay, lengthy working hours, heavy workloads, and a lack of opportunity for training and professional growth [18].

The provision of high-quality healthcare services is largely dependent on nurses and midwives, who also provide care for mothers, babies, and children, administer life-saving vaccines, provide health advice, and look after the elderly. There is a lack of nursing and allied health professionals in Ukraine, like all other European countries, and the Middle East [19–21].

When comparing with Pakistan, the result showed that child health care is being provided with specialist doctors as well as mostly by general medical practitioner but the situation is better than in Ukraine. Both the physical infrastructure and the workforce have steadily risen to support public health initiatives. The overall number of beds available in these healthcare institutions is expected to be 123394, and they include 1201 hospitals, 5518 basic health the facilities, 683 rural health facilities, 5802 dispensaries, 731 maternal & child health clinics, and 347 TB centers. Additionally, the population is receiving primary healthcare services from about 95000 Female Health Workers through the health houses. Pakistan has greater training and development resources than Ukraine [22].

Dr. Poonam Khetrapal Singh, Regional Director, WHO South-East Asia, assumed on World Health Day that it is imperative intensifying the efforts in order to ensure that the workforce of doctors, nurses, and midwives has the power, abilities, and support to attend to all people's health needs. To attain health for everyone by 2030, South-East Asian nations must step up efforts to develop and increase their cadre of nurses and midwives by 1.9 million [23, 24].

Status of Infrastructure, Equipment and Supplies

There have long been problems with the supply and maintenance of medical equipment especially in child healthcare hospitals. The majority of the equipment has been in operation for 20 to 25 years, far beyond its useful life, and the pace of replacing aging and damaged equipment is fairly sluggish. During the COVID-19 pandemic, there were 665 fewer hospital beds available per 100,000 persons in 2019 than there were in 2000. Hospital bed averages for Ukraine have continued to be higher than those for the EU and WHO's European Region. This may be due to the lack of effectively and efficiently use of available beds. This shows inappropriate training and development of health care staff resulting overcrowding in terms of hospital facilities and unneeded hospitalisations and shortage of equipment’s and medical supplies. In addition, the COVID-19 epidemic has made it clear that Ukraine's hospitals need to be reorganised [25].

While a different research carried out in Romania revealed that the number of hospital beds has been steadily declining over the last 30 years. There were 4630 beds for neonates and preterm infants and 7666 beds for children. Although over the past 30 years the infant mortality has steadily declined in Romania. It continues to be the highest in the EU. The most thorough indicator of a health system's effectiveness is infant mortality. Even if there have been significant advancements in children's healthcare, more has to be done to guarantee a higher standard of care for our country's future, both in terms of infrastructure and human resources [26].

Studies carried out in Bangladesh revealed that the healthcare facilities there were inadequate in many of areas, particularly in the areas of medical supplies and equipment, diagnostic abilities, and medical supplies inventory [27, 28].

Status of burden of disease

The available statistics indicate a decrease in the infant mortality rate from 7.3 in 2019 to 7 in 2021, and a similar trend for the under-5 mortality rate and neonatal mortality rates in Ukraine. However, the decline in neonatal

mortality rates is slow. The infant mortality rate and under-5 mortality rate have improved significantly from 17 and 19 per 1,000 live births in 1990 to 7 and 8 per 1,000 in 2019. In contrast, Pakistan's infant mortality rate was much higher at 57.998 deaths per 1000 live births in 2021 and 59.109 deaths per 1000 live births in 2020. Therefore, Ukraine has better health indicators than Pakistan [29].

When comparing with other European countries, statistics showed that Ukraine has a higher infant mortality rate of 7% than neighbouring European nations like Belarus and Russia, which had infant mortality rates of 2% and 5%, respectively. Similar to this, the death rate for children under the age of five is 8% in Ukraine, 3% in Belarus, and 6% in Russia. In Russia, Belarus, and Ukraine, the death rate for children aged 5 to 14 is 2%, 1%, and 2%, respectively. In Russia, 6% of infants are born weighing less than 2500g, compared to 5% in Belarus and 6% in Ukraine [30, 31].

The danger for children in Europe and North America is 14 times higher than that in sub-Saharan Africa, where there are 74 fatalities for every 1,000 live births, the worst mortality rate in the world. In 2020, the global under-5 mortality rate dropped to 37 fatalities for every 1,000 live births. The main causes of death in children under the age of five include preterm birth complications, birth asphyxia or trauma, pneumonia, diarrhoea, and malaria. With access to low-cost health and sanitation programs, all of these illnesses might be prevented or cured [32, 33]. The disparity in mortality between Europe and North America and sub-Saharan Africa may be ascribed to issues like poverty, a lack of proper healthcare facilities, and restricted access to clean water and sanitary facilities. These elements contribute to a greater prevalence of illnesses and diseases that may be avoided, which raises the mortality rates of children in sub-Saharan Africa.

Compared with Asia-Pacific countries the literature claims that the infant mortality rate in lower-middle and lower-income Asia-Pacific nations decreased from 54.4 deaths per 1,000 live births in 2000 to 27.2 in 2018. In a similar vein, over the same time period, upper-middle income Asia-Pacific nations reported a drop from 18.2 to 10 fatalities per 1,000 live births. Eastern Asian nations have lower infant mortality rates than South and South-East Asian nations. The cities of Hong Kong, Japan, China, Singapore, and the Republic of Korea had the lowest rates in 2018, with three fatalities or fewer per 1,000 live births. These results show how far Asia-Pacific nations have gone in lowering infant death rates, especially in lower-income areas [34, 35].

Vaccination status

The WHO's objective criteria for herd immunity for some of the most severe illnesses were never reached in Ukraine, which has one of the lowest vaccination rates in all of Europe. 20% of Ukrainian youngsters were not properly immunised against measles in 2021, and 13% were not poliovirus-protected [36, 37].

When comparing with other European countries, the literature showed that children vaccinated against measles in 2021 were 99.8% in Hungary, 99.5% in Portugal, 97.3% in Russia, 96.1% in Turkey, 96% in Finland, and 80.3% in Poland. By the year 2021, virtually all of Hungary's youngsters have received the measles vaccine. To eradicate the illness and halt its transmission to people in high-risk categories, it is advised that at least 95% of the populace take the measles vaccination [38, 39]. Ukraine's poor measles and poliovirus immunisation rates increase the risk of outbreaks and susceptibility. Compared to other European countries with greater measles vaccination rates, Ukraine needs more vaccine promotion and access activities. Herd immunity protects persons who cannot acquire vaccines due to medical conditions or age. Thus, high immunisation rates are essential for individual and group health. Ukraine's poor vaccination rates are due to vaccine aversion, misinformation, and limited healthcare availability. Health education campaigns targeting parents and medical professionals should promote vaccination's benefits and safety. Improved healthcare systems and universal vaccine access should be implemented. To raise vaccination rates in Ukraine, a public health priority, the government, medical specialists, and the public must work together.

In terms of polio vaccine, according to the World Health Organisation, the whole continent of Europe was deemed polio-free in 2002. However, this status requires continued polio immunisation of children. In 2018, 98 percent of children in Turkey and 99.9 percent of youngsters in Hungary got the polio vaccine. In contrast, just 71% of youngsters in Ukraine got a polio immunization this year [40, 41]. Low vaccination rates in Ukraine are the result of a number of issues, including widespread vaccine reluctance, which has been exacerbated in part by social media campaigns that propagate false information about vaccines and erode public confidence in Ukrainian institutions.

In Ukraine, outbreaks of illnesses that are preventable by vaccination have lately occurred as a consequence of low vaccination rates. The greatest outbreak in Europe in more than ten years, over 115 000 cases of measles and 40 fatalities connected to the disease were documented in Ukraine between 2017 and 20. A confirmed epidemic of type 2 vaccine-associated paralytic poliovirus occurred in 2021. More than 20 kids were found to have poliovirus, and two of them had acute flaccid paralysis. While there were significant increases in measles

outbreaks in the other European Economic Area in 2017 and 2018, with about 3.5 thousand cases. Measles rates peaked in 2019 at a lesser rate than they did the two years before, but the current rise in cases may be linked to the growth of anti-vaccination sentiment throughout several European countries. However, the monthly reported cases of measles were at their lowest levels in the years 2020 and 2021, which might have been impacted by increased social isolation measures implemented in response to the COVID-19 pandemic and people's belief in vaccination as a preventative measure [42–44].

Status of Healthcare spending

Paediatric healthcare in Ukraine has substantial budget issues, which contribute to a lack of medical staff, equipment, and supplies. Furthermore, a high frequency of avoidable children illnesses has been attributed to a lack of public knowledge about paediatric health and prevention. In 2021, the public spending ratio the proportion of state spending to GDP – varied across the member states of the European Union in relation to other European nations. The largest public spending per GDP was in Belgium (54.91%), followed by Portugal (48.15%), Poland (44.2%), Bulgaria (40.425%), and Hungary (47.92%) [45,46]. The well-being of children in Ukraine is negatively impacted by the inadequate financing for paediatric healthcare. This problem is probably exacerbated by the low public expenditure on healthcare in comparison to other European nations since less money is available to invest in enhancing the healthcare system. It is crucial that Ukrainian politicians give priority to increasing public expenditure on healthcare, especially paediatric healthcare and must remember that public healthcare expenditure is only one element that influences the quality of healthcare. Other elements, such the effectiveness of healthcare systems and the accessibility of medical staff and resources, are also quite important.

When comparing the results with the countries among the OECD, the United States spent the most on healthcare per person in 2021. Germany, which came in second with spending of $12,318 per person, was well behind the United States in terms of healthcare spending at the time. On a per capita basis, the Netherlands, Switzerland, and Norway are among the top five nations. The United States spends the most of its GDP on health care, almost 19 percent of it, making it the country with the highest health care spending [47]. This comparison create a helpful way to assess a nation's commitment to the welfare of its population is to compare healthcare expenditures among nations. Despite having the largest healthcare expenditure per capita and GDP, the United States does not have the best healthcare results when compared to other high-income nations. The results show that better health outcomes are not necessarily associated with more healthcare expenditure. Because of all this, policymakers must take into account not just the quantity of money allocated to healthcare, but also how effectively those resources are distributed and used to provide the population with high-quality treatment.

But the situation is different when comparing Ukraine with low- and middle-income countries and the European region. The literature showed that Ukraine spends more per capita on health than lower-middle-income countries ($426) but less than the WHO European Region average. Health expenditure as a proportion of government spending increased to 6.8% in 2018 from 6.8% in 2008. In 2018, Ukraine spent 3.7% of its GDP on health, greater than the LMIC average (2.8%) but less than the WHO European Region (4.9%) and the EU (5.9%). Private health spending was 51% in 2018, up from 39.1% in 2006. This is an increase from 39.1% in 2006. Private expenditure, which is nearly completely out-of-pocket, has the potential to bankrupt families while also preventing patients from receiving required treatment. Many people may become bankrupt due to medical expenses. In 2019, 16.7% of Ukrainian families spent catastrophically on health care, which was more than in many other WHO European Region nations. Coverage gaps in publicly funded health care cost patients a lot of money. Different economic developments, political systems, and health care systems, among other things, may be blamed for the disparity in health spending and funding between Ukraine and other nations.

Conclusions and Implications

Numerous obstacles that affect children's health and welfare exist in paediatrics in Ukraine. Despite these difficulties, there are a number of opportunities for advancement in paediatrics that might help to enhance the quality of child healthcare in the nation.

1. The inadequate healthcare infrastructure is one of the main issues in Ukrainian paediatrics. Paediatric experts, healthcare facilities, and medical supplies are in limited supply. Children's health suffers as a consequence of lengthy appointment wait times, insufficient diagnosis, and treatment. Additionally, the advancement of paediatric healthcare is hampered by a lack of funding for the study and development of novel therapies and medications.
2. The high new-born and child mortality rate is still another serious issue. This is caused by a number of things, including insufficient nutrition, a lack of access to clean water and sanitary facilities, and avoidable illnesses

including pneumonia, diarrhoea, and TB. Neonatal mortality is very high, with the majority of fatalities happening within the first 24 hours following birth.

3. The COVID-19 epidemic has exacerbated the issues that Ukraine's children's healthcare system already faced. The pandemic has reduced the number of regular vaccines, made it more difficult to access medical facilities, and disrupted the delivery of crucial services. These factors have increased the number of avoidable diseases and the strain on the already overburdened healthcare system.

4. Despite these issues, there are still many possibilities able to improve paediatrics in Ukraine. The government has launched a variety of projects in an effort to enhance children's health care. These include creating a national strategy for women's and children's health care, raising the health care budget, and enhancing the infrastructure for health care. Additionally, a number of non-governmental organisations and foreign assistance organisations are striving to enhance children's healthcare in the nation.

5. The emergence of telemedicine and e-health services is one of the most important opportunities for advancement. This will provide kids in isolated and rural locations access to specialised treatment while also addressing the scarcity of paediatric experts. Additionally, telemedicine may assist cut down on appointment wait times and increase the effectiveness of healthcare delivery.

6. The expansion of services for maternity and paediatric healthcare is still another opportunity. This entails expanding access to maternity care, delivering better prenatal care, enhancing nutrition, and lowering the incidence of illnesses that can be prevented. The health results for children in the nation may also be greatly improved by expanding vaccine access and fostering public health education.

In conclusion, the field of paediatrics in Ukraine faces a number of obstacles, the most significant of which are a shortage of first-quality medical facilities and a high death rate among infants and young children. But there are things that can be done to make the situation better, such as expanding telemedicine and e-health services, improving care for mothers and children, and spending more money in research and development. By addressing these concerns and providing financing for these opportunities, the country has the potential to greatly enhance the physical health of its children as well as their overall level of happiness.

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