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Vaccination of pregnant women against COVID-19 under martial law: a narrative review

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Abstract

Background: Global vaccination programs against the coronavirus illness of 2019 (COVID-19) have been established as the primary measure to minimise and control the effects of the COVID-19 pandemic. During pregnancy, it is assumed that the expectant mother and her fetus are both in danger from the possibility of a viral infection.

Aim: to evaluate the safety and effectiveness of vaccination against COVID-19 for pregnant women and determine the impact of vaccination on pregnancy outcomes.

Methods: In this review, English studies from common databases such as Pubmed/MEDLINE, Web of Science, Scopus, and the Cochrane Library with the keywords "Vaccination," "pregnancy," and "pregnant women," combined with keywords, involving "COVID-19," were involved. The end date for this review is March 2022.

Scientific novelty: The main objective of this paper is to evaluate the effect of vaccination of pregnant women against COVID-19. Even though many studies assessed the efficacy of vaccination against COVID-19, most failed to determine the safety and effectiveness of COVID-19 vaccination for immunocompromised patients, especially pregnant women. Additionally, the impact of COVID-19 vaccination on neonatal outcomes was evaluated.

The practical significance of the obtained result: Concerns have also been raised about potential risks associated with vaccination during pregnancy or breastfeeding. Given these uncertainties, it is important for healthcare providers to carefully consider the risks and benefits of COVID-19 vaccination for pregnant women and their babies. Further research is needed to better understand the effects of vaccination on perinatal outcomes and to inform clinical decision-making around vaccine use in this population.

Conclusion: The COVID-19 vaccination is a safe and effective way to protect pregnant women from the virus. The benefits of getting vaccinated outweigh the risks, as pregnant women are at an increased risk of severe illness and complications from COVID-19. The Centers for Disease Control and Prevention (CDC) recommends that pregnant women get vaccinated, and many healthcare providers also recommend it. However, it is important for pregnant women to discuss their individual situation with their healthcare provider before making a decision about vaccination. Overall, getting vaccinated can help to protect both the mother and her unborn child from COVID-19.

Keywords: Vaccination, coronavirus, COVID-19, pregnant women, Neonatal outcomes.

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Introduction

Several COVID-19 vaccinations have been approved for emergency use to prevent severe COVID-19 disease caused by the SARS-CoV-2 virus. They have played an essential role in improving clinical outcomes and reducing the severity of the pandemic. Moreover, a unique immunisation strategy based on mRNA vaccines was developed during the pandemic [1,2]. The severity of the pandemic is globally recognised, and preventative measures such as good hygiene, masking, social distancing, and regular monitoring of health conditions are in place. As the pandemic spread worldwide, scientists worked on numerous vaccinations in order to help boost herd immunity and reduce the danger of viral infection [3,4].

Pregnancy is usually associated with a high incidence of various viral infections [5,6]. Immune changes during pregnancy may reduce the effectiveness of cell-mediated immune responses to infection [6]. Pregnant or recently pregnant women have an increased chance of suffering from a severe form of Covid-19, stillbirth, and preterm birth, according to the Centers for Disease Control and Prevention (CDC) [7,8]. Pregnancy is a risk factor for acquiring a severe SARS Cov-2 infection, according to the Society for Maternal and Fetal Medicine (SMFM) and the American College of Obstetricians and Gynecologists (ACOG) [9]. Pregnant women should be notified of the increased severity of covid-19, which includes invasive ventilation and intensive care unit admission when compared to non-pregnant women, and encouraged to take preventative measures to lower their risk of infection, such as getting the covid-19 vaccine to diminish their risk of developing a serious illness [10].

Research Problem

Most people have some fears about the vaccination against COVID-19 and have difficulties in finding good scientific evidence that help them to determine whether COVID-19 vaccination is safe and effective. These fears are doubled for immunocompromised individuals such as HIV patients and pregnant women. The lack of knowledge about the effects of immunisations during pregnancy and the safety of fetuses are two of the most common reasons pregnant women do not receive immunisation.

Research Focus

The safety and effectiveness of the approved COVID-19 vaccinations during pregnancy and their effects on the mother and fetus' immune systems were the main topics of this review.

Research Questions

1. What are the types of COVID-19 vaccines?
2. Is the vaccination against COVID-19 safe and effective for pregnant women?
3. What is the impact of vaccination against COVID-19 on pregnancy outcomes?
4. What is the risk of pregnant women being infected with COVID-19?

Research Aim

Therefore, this review was performed in order to evaluate the safety and effectiveness of vaccination against COVID-19 for pregnant women and to determine the impact of vaccination on pregnancy outcomes.

Research Methodology

General Background

The studies that were found using each set of keyword combinations were then pooled to create an impartial collection of publications. Studies and/or articles that weren't subjected to peer review, as well as proposals, procedures, reviews, letters, and opinions, were eliminated. The references include publications that were chosen in terms of their relativity to the topic. The research is concentrated on providing an overview of the effect of vaccination of pregnant women against COVID-19.

Data Analysis

In this review, English studies from common databases such as Pubmed/MEDLINE, Web of Science, Scopus, and the Cochrane Library with the keywords "Vaccination," "pregnancy," and "pregnant women," combined keywords involving "COVID-19," were involved. The end date for this review is March 2022.

Research Results

The result of the search using the chosen search strategy was 2367 articles. These articles to choose as well as the articles related to the topic were screened. A full-text screening of 344 articles after excluding the remaining article by title and abstract screening was accomplished. Finally, 51 articles to gather information about the topic and write this review were used (Figure 1).

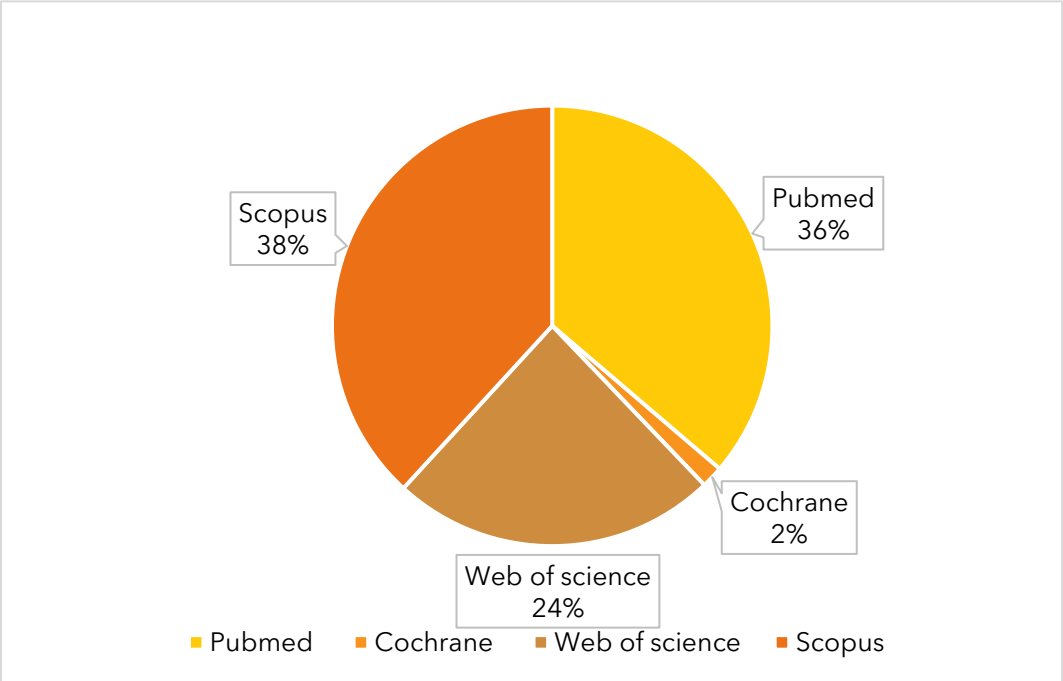

Figure 1. Research results

Literature review

The COVID-19

In late 2019, the COVID-19 outbreak first appeared in Wuhan, Hubei, China, and it has since quickly spread worldwide [11]. The virus responsible was discovered to be the 2019 new coronavirus [12]. The World Health Organization (WHO) later renamed this virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). WHO declared COVID-19 a pandemic and recommended aggressive action from all nations due to the infection's rapid spread and worldwide effects [13]. The discovery that SARS-CoV-2 may transmit from person to person through respiratory vay and close contact presented a significant challenge to public health as the infection's transmission rate accelerated [14].

Mild COVID-19 cases included such symptomatics as myalgia, fever, a sore throat, and malaise but no dyspnea, shortness of breath, or abnormal chest imaging that would suggest lower respiratory tract disease. Mild COVID-19 infection accounts for 81% of symptomatic infections [15]. During chest ex-ray or physical examination, patients with moderate illness show signs of lower respiratory disease, but they nevertheless maintain an oxygen saturation of 94% or more in room air at sea level. The critical condition is characterised by multiorgan deficiency, septic shock, and respiratory deficiency [16].

COVID-19 in pregnancy

It is generally acknowledged that particular respiratory infections, such as varicella pneumonia and H1N1, increase the risk of mortality and severe morbidity in pregnant women [17]. This includes an increased risk of developing a serious disease when infected with COVID-19-related viruses as well as other viral respiratory illnesses like influenza [18,19]. Regarding COVID-19, the limited information does not suggest that pregnant people women are more likely to acquire an infection or have severe morbidity (such as the need for ICU hospitalisation or fatality) than non-pregnant women [20,21].

Some research has raised questions about the possibility that pregnant women may be more vulnerable to COVID-19 because they may generally be more susceptible to respiratory infections [22]. According to the evidence, pregnant women are no more susceptible to this specific virus than the general public [23]. The non-pregnant and

pregnant populations have vulnerable subgroups; doctors must be aware of these high-risk groups and treat them appropriately. Individuals with pre-existing diabetes are particularly susceptible to the negative consequences of COVID-19 infection [24].

The pregnant woman experiences several physiological changes throughout most of the gestational period that mimic numerous disorders and raise her exposure to infectious diseases. Many organ systems change during pregnancy, but the cardiovascular and respiratory systems are most affected. Red blood cell mass and blood plasma volume rapidly elevate during pregnancy and reach a peak in the third trimester [25,26]. Physiological dilutional anemia appears when the volume of blood plasma increases beyond the mass of blood cells. Increased exhaustion is one of the symptoms of anemia in pregnancy, which is a major cause of morbidity. Lower extremities edema and tachycardia are two additional symptoms of physiologic morbidity brought on by the concomitant rise in heart rate and decreased systemic vascular resistance. Patients also enhance total minute ventilation in the respiratory system by increasing total tidal volume. Pregnancy-related physiological dyspnea is caused by respiratory alkalosis caused by increased ventilation throughout the pregnancy.

According to statistics, between 60 and 70 percent of women feel dyspnea and shortness of breath with exertion, with occurrence rates rising in the second trimester [27]. Diagnosing lung disease during pregnancy is challenging due to these physiologic changes. COVID-19 infection has a broad range of presenting symptoms, which makes this challenge more difficult. Regarding the presence of shortness of breath (30%) and cough (52%), symptoms of COVID-19 in pregnancy are comparable to infections in the general population. However, compared to the general population, pregnant women were less likely to suffer symptoms of diarrhea (14%), headache (41%), chills (38%), and fever (34%) [28] **(Figure 2)**.

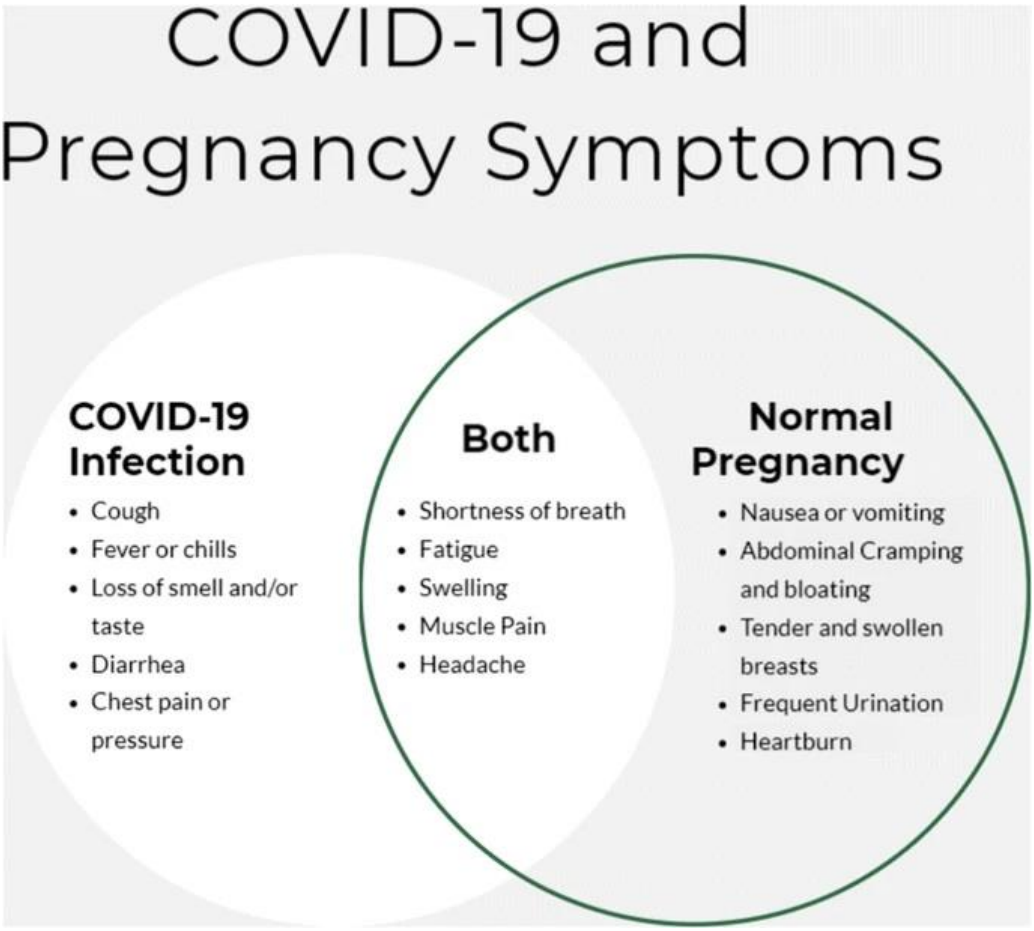

Figure 2. COVID-19 and pregnancy symptoms [29].

Pregnancy outcomes

Wei et al. performed a systematic review and meta-analysis in order to determine the relationship between the infection with COVID-19 during pregnancy and the outcomes of pregnancy. They involved forty-two articles,

including 438548 pregnant women. They found that COVID-19 in pregnancy is accompanied by preterm birth, stillbirth, preeclampsia, and maternal ICU admission compared with cases without COVID-19. Contrary to asymptomatic COVID-19, symptomatic COVID-19 was linked to a higher risk of premature birth and cesarean delivery [30]. The exact processes behind the relationship between preeclampsia and COVID-19 are still unknown. Researchers have found evidence that SARS-CoV-2 may cause renin-angiotensin system malfunction and vasoconstriction via binding to angiotensin-converting enzyme 2 receptors [31]. Most women had cesarean sections because of fetal distress and premature membrane rapture (PROM) to prevent vertical transmission and decrease unfavorable neonatal and perinatal outcomes [32,33]. Elective cesarean sections were also performed to reduce women's respiratory discomfort [32,34]. Pregnant women's most important laboratory results were Lymphocytopenia, increased liver enzymes, and leukocytosis. On chest CT scans, consolidation lesions, and sporadic ground glass shadows were the most often found abnormalities. Concerns have been raised about infection-related pre- or postpartum maternal deaths [35].

Neonatal outcomes

Clinical symptoms include fever, feeding intolerance, disseminated intravascular coagulation, birthing problems, bleeding, cyanosis, edema, rash, pneumonia, and dyspnea have been reported in neonates born from COVID-19-infected pregnant women [36]. Babies born to women with COVID-19 had a greater risk of admission to the neonatal intensive care unit (NICU) and stillbirth than babies born to women without COVID-19 [37,38]. The vertical transmission seems infrequent, and most babies born to mothers who caught COVID-19 during pregnancy are healthy. Most newborns with COVID-19 experience a modest illness course with unchanged outcomes. Yet, there are numerous reports of COVID-19 having a significant negative influence on the neonatal brain of infected newborns. Some follow-up studies imply that children born during the pandemic have a higher frequency of behavioral and neurodevelopmental issues [39].

COVID-19 vaccination

There are currently several types of COVID-19 vaccines that have been authorized for emergency use around the world. These vaccines work in different ways to help protect against the virus.

1. mRNA vaccines: These vaccines, such as Pfizer-BioNTech and Moderna, use a small ammount of genetic material called messenger RNA (mRNA) to instruct cells to produce a protein found on the surface of the virus. The mRNA method is ideally suited for the creation of vaccines against recently emerging viruses like SARSCoV-2 because of its flexibility, speedy development, safety, and powerful immunogenicity. MRNA vaccines against COVID-19 were effectively created at a rate never before achieved, building on significant technological advancement and advancement in the mRNA vaccine platform over the previous ten years. However, given that COVID-19 vaccines are the first mRNA vaccines to be approved for sale, some problems with potential large-scale manufacturing and the vaccine's long-term storage stability may arise [40,41].

2. Viral vector vaccines: These vaccines, such as AstraZeneca and Johnson & Johnson, use a harmless virus (such as adenovirus) to deliver genetic material from the COVID-19 virus into cells. This also triggers an immune response. The replication-deficient chimpanzee adenoviral vector chAdOx1 is used in chimpanzee adenovirus immunization. It is integrated with the surface spike protein's genomic code and has been genetically modified to match the SARS-CoV-2 spike protein [40].

3. Inactivated or killed virus vaccines: These vaccines, such as Sinovac and Sinopharm, use a dead or inactivated version of the COVID-19 virus to stimulate an immune response. So it cannot cause disease but still stimulates an immune response in the body. The killed vaccine for COVID-19 is made by growing large quantities of the virus and then treating it with chemicals or heat to render it inactive. This type of vaccine has been used successfully for other diseases such as polio, hepatitis A, and influenza. The killed vaccine remains an important tool in the fight against COVID-19 and will continue to be studied and improved upon as we learn more about this novel virus.

4. Protein subunit vaccines: These vaccines contain harmless pieces of proteins found on the surface of the COVID-19 virus to trigger an immune response. In the case of COVID-19, protein subunit vaccines use a piece of the spike protein found on the surface of the SARS-CoV-2 virus. This spike protein allows the virus to enter human cells and cause infection. To create a protein subunit vaccine, scientists first identify which part of the virus they want to target. In this case, they focus on the spike protein. They then use genetic engineering techniques to produce large quantities of just that part of the virus in a laboratory setting. Once enough of the spike protein has been produced, it is purified and used as the main component of the vaccine. When injected into a person's body, this purified spike protein triggers an immune response that helps protect against future infections [42].

One advantage of protein subunit vaccines is that they are generally considered safe and well-tolerated. Because they only contain a small ammount of the virus or bacteria, there is little risk of causing an actual infection.

Additionally, because they do not contain live viruses or bacteria, they can be safely given to people with weakened immune systems [43].

Several COVID-19 vaccines currently in development use protein subunits as their main component. These include Novavax's NVX-CoV2373 vaccine and Sanofi/GSK's adjuvanted recombinant protein-based vaccine candidate [44].

All of these vaccine types are effective at preventing severe illness and hospitalization from COVID-19. It is important for individuals to receive whichever vaccine is available to them in their area in order to help protect themselves and others from the spread of the virus.

COVID-19 vaccination in pregnancy

The recent recommendation about using the COVID-19 vaccine in pregnancy is that the vaccine should be used as early as possible for the maternal benefit due to the substantial rise in SARS-CoV-2-related mortality among pregnant women. It is essential to understand how COVID-19 vaccination affects pregnancy and, consequently, placental antibody transfer to provide vaccine recommendations for this population group [45]. A cohort analysis showed that humoral immunity developed during pregnancy, with reactivity and reactogenicity comparable to those seen in non-pregnant women; vaccine-induced antibody titers were the same in both groups of women. On the other hand, few studies have discovered decreased immunity during pregnancy in comparison to that seen in women who received vaccinations but were not expectant [45,46]. Prabhu et al. [47] studied 122 pregnant woman with SARS-CoV-2 and found that IgG level was 43.6% following the first dosage of mRNA-based vaccination; 98.5% following two doses. Besides, two weeks after the initial dosage of the vaccine, maternal IgG levels were noticeably increased each week by week.

Regarding the antibody transfer to the fetus, by four weeks after the first immunisation dosage, IgG antibodies were present in all but one cord blood sample.

Atyeo et al. [45] studied the concentration of the Fc portion of the antibodies after mRNA-based COVID vaccination. After the first dosage, they found that Fc receptor antibody concentrations were considerably lower in pregnant women than in non-pregnant women. After the second dosage, Fc receptor antibody concentrations rose substantially but remained lower than in non-pregnant women.

Discussion

Several published studies reported that COVID vaccination was very effective in reducing the risk of infection and the severity of the disease. A wide-scale analysis of Scotland population was performed by Goldshtein et al. [48]. They included 126149 unvaccinated and 18399 vaccinated pregnant women. About 77% of COVID infections, 90% of hospital admissions, and 98% of critical care admissions were in the unvaccinated group. A previously published study also examined the efficacy of maternal vaccination against covid-19-related hospital admittance in newborns during the first six months of life. The incidence of hospital admission with COVID was significantly higher in infants whose mothers were not vaccinated. They discovered that maternal vaccination during pregnancy reduced the risk of covid-19-related hospital admittance in children under 6 months by 61%.

Regarding the effect of COVID vaccination on perinatal outcomes. Several studies reported that the perinatal adverse effects did not increase after maternal vaccination. Perinatal outcomes refer to the health outcomes of both mother and baby during pregnancy, childbirth, and postpartum. Various factors can affect these outcomes, including maternal health status, environmental factors, and medical interventions such as vaccination.

Theiler et al. [49] reported that the incidence of preterm birth was 9.3% in the vaccinated woman and 8.5% in the unvaccinated woman. The rates of cesarean deliveries were 31.4% in the vaccinated woman, unvaccinated 29.8%. NICU admission: vaccinated 0.07%; unvaccinated 0.6%. The difference in these perinatal outcomes was not significant between both groups.

Kharbanda et al. [50] reported that the incidence of spontaneous abortion was 8.6% SAB that occurred within 28 days of vaccination.

Concerning the adverse events of COVID-19 side effects in pregnancy. Typically minor to severe symptoms follow the covid-19 vaccination, and they start to appear three days after receiving the vaccination. The majority start the day after the immunisation and pass in one to two days. The second dose is linked to more serious and regular side effects. Pregnancy-related vaccine adverse effects appear to be comparable to those in non-pregnant individuals, with pain at the injection site, fatigue, headaches, and myalgia being the most common signs.

Conclusions and Implications

1. COVID vaccination in pregnancy is a safe and effective way to protect both the mother and the developing fetus from the virus.

2. The Centers for Disease Control and Prevention (CDC) recommends that pregnant individuals receive the COVID vaccine, as they are at an increased risk of severe illness and complications from COVID-19.
3. Studies have shown that COVID vaccines do not increase the risk of miscarriage or other adverse pregnancy outcomes.
4. Pregnant individuals who contract COVID-19 are at a higher risk of preterm birth, stillbirth, and other complications, making vaccination even more important.
5. Vaccination during pregnancy can also provide passive immunity to newborns, who are unable to receive the vaccine themselves until they are at least 12 years old.
6. It is important for healthcare providers to educate pregnant patients about the benefits of vaccination and address any concerns or questions they may have.
7. By getting vaccinated during pregnancy, individuals can help protect themselves, their unborn child, and their community from the spread of COVID-19.

Declarations

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Data sharing statement

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

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Implementation of digital technologies in the medicine of the future

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Abstract

The parallel development of digital and telecommunication technologies in recent years has created ample opportunities to improve traditional healthcare delivery systems. New models of healthcare services are supported by scientific developments and digital innovations.

Objectives: To improve doctors' expertise and healthcare managers with the main achievements of digital technologies introduction in practical medicine and the possibilities for further development of technologies in this area.

Methodology: A review of articles from professional peer-reviewed journals in the online medical literature search system MEDLINE from the US National Library of Medicine for 2018-2022 was conducted. The article concerns the use of digital innovations in clinical medicine, their achievements in oncology, cardiology, medical imaging and other healthcare fields.

Results: The article discusses the main digital strategies that are part of the practical work of doctors and create new workflows and interactions between patients and specialists of medical institutions. Attention is paid to the advances in computer technology and the challenges they pose to the quality of medical care. The introduction of telemedicine, problems of validation of results and clinical use of artificial intelligence applications, as well as opportunities for their development in the future are discussed.

Conclusion: New technologies, including artificial intelligence algorithms, machine learning, image recognition, radiomics, and telemedicine, are creating the prerequisites for the development of new forms of healthcare delivery. The combination of telemedicine, server-based applications, and machine learning algorithms can provide a synchronised solution to the challenges faced by modern society in ensuring a healthy future around the world.

Keywords: artificial intelligence; machine learning; radiomics; telemedicine; computer model; healthcare;

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Introduction

The widespread introduction of digital technologies in modern medicine in recent years has created a favourable atmosphere for reviewing possible directions for future clinical trials. New theoretical advances and clinical observations pose new challenges in the healthcare sector. The issues of disease surveillance, timely and early detection, improving the efficiency of diagnosis and treatment, search for new methods of treatment and rehabilitation, bringing healthcare closer to the patient and personalising medicine are being rethought.

Research Problem

The factors of digitalisation's impact on the patient-physician relationship need to be studied, as well as the impact of computer technology on the ability to predict the course of diseases and the state of public health. The limits of artificial intelligence application in diagnostics, treatment planning, and patient monitoring, as well as the ethics and transparency of the impact of machine learning systems on the work of healthcare institutions are being discussed.

Research Focus

The ever-increasing flow of data in the form of clinical images, continuous biometric data, and IoT devices is driving a steady increase in the number of studies on the impact of digital technologies on the state of future medicine. Large volumes of data that cannot be processed by traditional methods of human intelligence have significant potential to expand both theoretical knowledge of pathogenic processes in the human body and the practical application of machine learning systems in the diagnosis and treatment of patients.

Research Aim and Research Questions

Improving the familiarity of doctors and healthcare managers with the main achievements and challenges of implementing digital technologies in practical medicine will contribute to the further development of technologies in the provision of medical services to the population. To achieve this goal, it is necessary to find answers to the following questions:

1) What are the main digital strategies that are part of doctors' practice and how do they affect the interaction between patients and healthcare institutions?

2) How computer technologies used in healthcare delivery processes affect the quality of medical care.

3) What has already been implemented in the field of clinical application of artificial intelligence and telemedicine technologies, what prospects for their development are expected in future research.

Research Methodology

General Background

The growth of interest in digitalisation is clearly illustrated in Figure 1, which shows the number of publications in the US National Library of Medicine over the past 20 years. The number of such publications for the key words “digital technology healthcare” has increased from 3-5 per year at the beginning to 1276 this year.

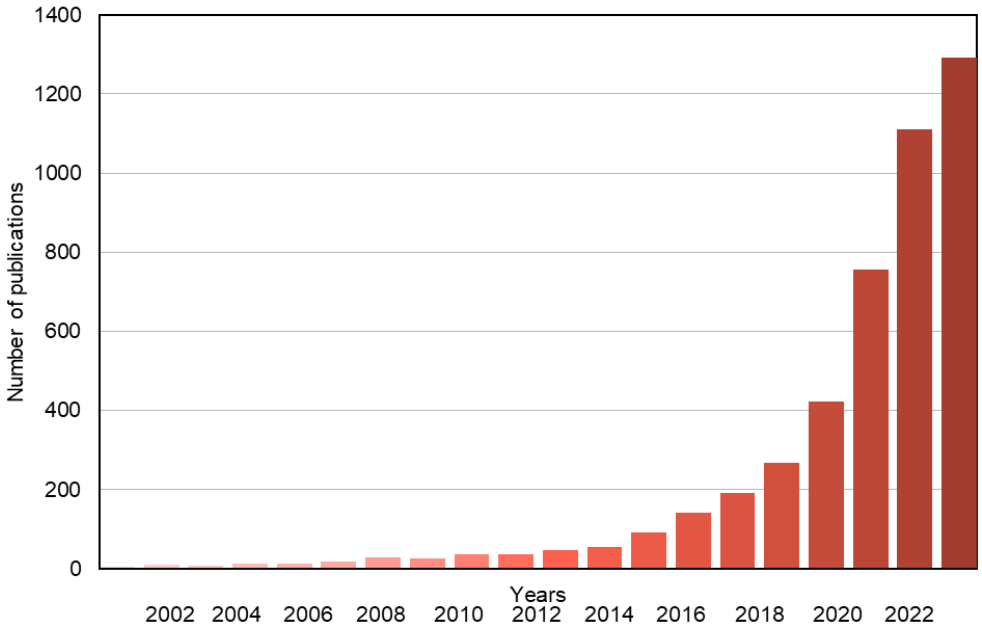

Figure 1. **Dynamics of publications concerning the topic over the past 20 years**

Data Analysis

To address these research questions, articles from professional peer-reviewed journals using the online medical literature search system MEDLINE from the US National Library of Medicine for 2018-2022 were reviewed. The limitations of the last five years are due to significant technological changes that make it incorrect to compare the capabilities of a decade-old machine park with modern computer equipment. The genders were selected by keywords: "digital technologies", "healthcare", "machine learning", "and computer model". Preference was given to review articles with the maximum coverage of the use of digital innovations in clinical medicine; there were no restrictions on the healthcare sector or the choice of medical specialties. Purely technical articles describing the mathematical justification for the choice of computer technologies were excluded from the review in order to keep the review accessible to practicing physicians and healthcare managers.

Research Results

The rapid introduction of digital changes in the field of medicine is based on artificial intelligence, the development of new mathematical algorithms for data processing, the development of consumer technologies, and the improvement of communication systems. Here are the definitions of the main concepts in the field of artificial intelligence [1], in hierarchical order:

- Artificial intelligence is the ability of a machine to imitate intelligent human behaviour: to learn, solve problems, and find the relationship between facts.
- Machine learning is a branch of artificial intelligence that enables programs to learn solely from collected data without explicit human programming.
- Representational learning is a type of machine learning that algorithmically explores the features necessary for data classification.
- Deep learning is a branch of machine learning that uses multilayer artificial neural networks to solve various problems. The definition of "deep" emphasises the fact that learning goes throughout the entire depth of the neural network, rather than concentrating on any specific level of it.

The results of the distribution of the selected sources by topic are shown in Figure 2. The following presentation of the information is divided into three subsections, in accordance with the research objectives.

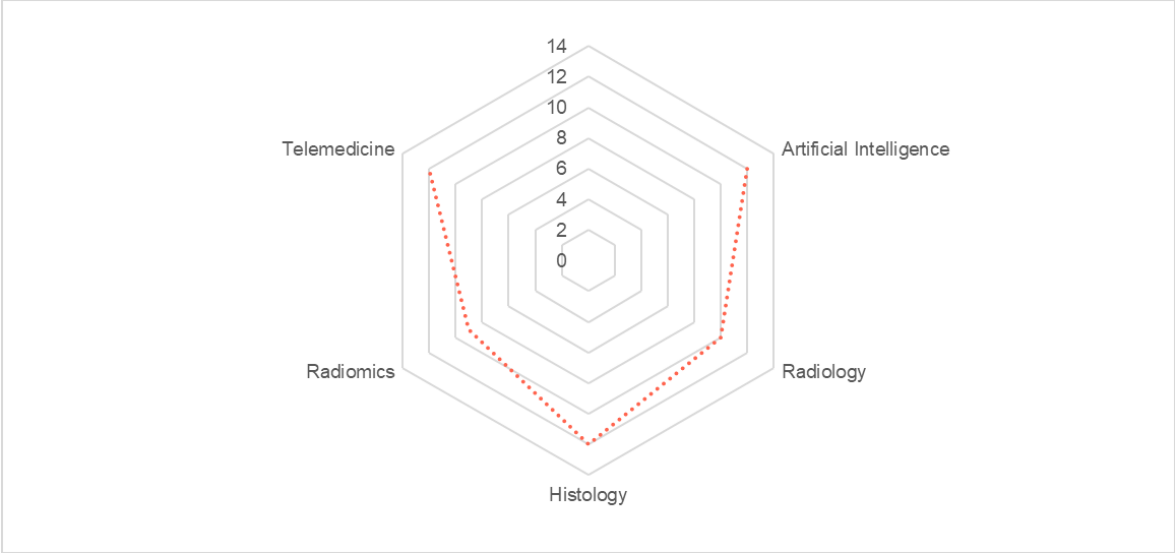

Figure 2. Breakdown of the number of publications by topic

Key digital technologies

Analysing the benefits that these modern computer technologies provide to the healthcare system it is visible that: while positively assessing the overall impact of artificial intelligence, many researchers [2-4] consider the simplification of the most common routine tasks of healthcare professionals to be the overall effect of digitalisation. According to H. Shimizu, K. Nakayama [5], deep learning algorithms have revolutionized practical oncology in the field of medical image analysis of clinical radiology and histopathology and successfully solve the problems of image classification in oncodermatology. The use of digital technologies not only eliminates routine human labour, but also reorients the work of image classification specialists to manage a larger volume of individualised care, requiring their attention only in cases that were not classified by artificial intelligence.

Deep learning algorithms can dramatically affect almost all aspects of oncology [6], from improving diagnostics to personalising treatment and discovering new anti-cancer drugs. Drawing on the development of digital technologies, A. Ibrahim et al. point out [7] that new knowledge about the complex nature of breast cancer and the availability of individualised treatments open up fundamentally different possibilities for diagnosing and treating this pathology. If a computer model can provide a better life expectancy prediction for a particular patient than existing risk stratification systems, it will be widely used in the future.

D.A. Hashimoto et al. [8], discussing the use of artificial intelligence in anaesthesiology, summarise six promising areas of its application: 1) monitoring the depth of anaesthesia, 2) control of medical anaesthesia, 3) prediction of intensive care risks, 4) ultrasound assistance in regional anaesthesia, 5) intraoperative pain relief, and 6) operating room logistics. Artificial intelligence demonstrates a decrease in the number of errors in clinical practice, not because it has surpassed humans, but because it narrows the field of attention for a specialist, allowing him or her to focus on the main thing. The authors are confident that the development of technologies that can help monitor the depth of anaesthesia, support drug infusions, or predict hypotension during surgery will allow practicing anaesthesiologists to be more efficient and effective.

Evaluating some of the applications of artificial intelligence methods in cardiology to date, K.W. Johnson et al. [9] identify how cardiovascular medicine can use artificial intelligence in the future. As the amount of possible patient data continues to increase due to the introduction of new research into the clinic, artificial intelligence systems will soon become an integral part of clinical practice. Algorithms will allow for the better treatment choices, eliminating much of the unproductive work of a cardiologist.

After considering the applications, potential limitations, and challenges of computer technology, R. Wang et al. [10] highlight the future prospects of artificial intelligence in the context of reproductive medicine. A medical expert system based on diagnostic algorithms will become the most important tool that can help practitioners solve complex medical problems.

In the era of universal digitalisation, the rapid development of artificial intelligence brings new ideas to forensic medicine [11]. Y.T. Fang et al. in their work present the results of many studies of forensic experts in recent years based on artificial intelligence technology, such as face recognition, age and gender identification, DNA analysis,

postmortem interval estimation, identification of injuries and causes of death, demonstrating the feasibility and benefits of using artificial intelligence technology to solve problems of forensic practice.

Computer image recognition

A classic example of the effective use of digital technologies in healthcare is the analysis of data obtained from medical imaging systems, among which, due to their prevalence, radiological images predominate [12-14]. The potential for computer technology to help analyse and interpret X-rays is of particular value, as X-rays are the most common imaging test performed in most medical facilities.

The progress of digital technologies in clinical medicine has made it possible to improve the level of diagnosis of bone and joint fractures of the extremities through the use of multi slice spiral computed tomography post-processing technology. W. Yang and F. Wang [15] conducted routine plain film X-ray radiography in 80 adult patients, followed by a computerised examination. The frequency of pathology detection on X-rays was 69%, and after applying post-processing technologies to computed tomography scans, the frequency of diagnosed pathology was 96%, 98%, and 99% in these 3 groups, respectively.

The role of artificial intelligence systems is vividly illustrated in the work of A. Rodríguez-Ruiz et al. 16, when they compared the effectiveness of breast cancer detection based on a retrospective cross-sectional multicenter study of 240 women. 14 qualified radiologists evaluated the standardized reporting system for analysing breast images for the likelihood of a malignant process twice - independently and with the support of an artificial intelligence system. Decision support included interactive interactions: a click on a breast area provided a computerised estimate of the local cancer probability, traditional lesion markers were used for algorithmically detected abnormalities, and an estimate of the cancer probability based on the examination. As a result, sensitivity with AI-assisted systems increased from 83% to 86% ($p = 0.046$), specificity tended to improve (79% vs. 77%, $p = 0.06$), and the time to analyse one case was similar (unassisted - 146 seconds; AI-assisted - 149 seconds; $p = 0.15$).

In order to determine the potential of artificial intelligence to improve the accuracy of mammography screening by reducing the number of missed cancers and false positives, an international competition was held between the United States and Sweden to develop algorithms [17], with more than 1,100 participants. To train and test the algorithms, 144,231 screening mammograms of 85,580 American women and 166,578 examinations of 68,008 Swedish women were used. An ensemble method was developed and evaluated that combines the best artificial intelligence algorithms and radiologists' judgment. As a result, the most effective algorithm achieved an area under the error curve of 0.858 (USA) and 0.903 (Sweden) and a specificity of 66.2% (USA) and 81.2% (Sweden), while maintaining sensitivity values typical of general radiologists. The combination of a set of selected best artificial intelligence algorithms and radiologists' assessments allowed to achieve significantly better specificity (92.0%) with the same sensitivity.

The introduction of digital artificial intelligence systems is gradually changing the clinical workflow. E.J. Hwang et al. [18] in their study present the results of the development of a deep learning algorithm that can classify normal and abnormal chest X-ray results with major chest diseases, including lung malignancies, active tuberculosis, pneumonia, and pneumothorax. The developed algorithm demonstrated significantly higher efficiency than that of all doctors both for image classification (0.983 vs. 0.814; $p < 0.005$) and for lesion localization (0.985 vs. 0.781; $p < 0.001$). The same picture can be observed in the work of H. Yoo et al. [19], when an artificial intelligence algorithm based on deep learning improved the sensitivity of lung cancer diagnosis for residents (from 0.61 to 0.72; $p = 0.016$) and specificity for radiologists (from 0.17 to 0.24; $p < 0.001$) in detecting pathology. Thanks to artificial intelligence, doctors were able to recommend more chest CT scans to patients with cancer (from 54.7% to 70.2%; $p < 0.001$), and the percentage of incorrectly prescribed tests for healthy patients decreased from 16.7% to 11.7% ($p < 0.001$).

Promising possibilities for detecting brain metastases through the introduction of high-tech algorithms are demonstrated by M. Zhang et al. [20] in a retrospective study of 361 brain scans in 121 patients. First, a computer model detected abnormal areas of high intensity that could be tumour metastases, and at the second stage, the model's classifier analysed the data to reduce the number of false positives. Testing of the brain images demonstrated 96% sensitivity, with 20 false-positive metastases per scan and 0.24 false-positive metastases per slice. The authors conclude that the deep learning method has a high potential for detecting brain metastases with high sensitivity and sufficient specificity. This result is also confirmed by the work of P. Azimi et al. in [21], in which the artificial neural network showed the best result of 95.3% accuracy in similar conditions. We can be sure that the introduction of artificial intelligence technologies in the future will significantly improve the quality, value and efficiency of the radiology service in providing medical care to the population and preserving the public health of future generations [22, 23].

The rapid development of digital technologies has created a new area of computer image analysis called radiomics [24]. If we think of a diagnostic image as a digital array, then, in addition to the features visible to the

researcher, algorithmic analysis can be directed to the quantitative characteristics of the array and thus obtain valuable diagnostic information. Understanding the main types of radiomarkers can facilitate the perception of the results of modern research and their selection for practical clinical use. Here is a brief description of the most common radiomarkers, the full list of which is far beyond the scope of this review and requires special mathematical knowledge. The main radiomic features include: statistical descriptors of the gray-level histogram (mean, maximum, minimum, variance, and percentiles), second-order features (symmetry and kurtosis, which describe the shape of the data intensity distribution), texture features (absolute gradient, grey-level matrices, lengths of segments and zones by grey level, neighbourhood tone matrices), features of parameterized and autoregressive models, fractal analysis data (dimensionality, lacunarity), features based on transforms (Fourier, Gabor and Haar wavelet transforms, quadrature mirror filters) and features based on shape (compactness, sphericity, density). Thus, in addition to morphological features visible to humans, many hundreds of radiological features correspond to one medical image, which greatly expands the analysis capabilities but requires complex mathematical calculations [24, 25].

Recent studies [26] have demonstrated the potential usefulness of radiomics for staging liver fibrosis, detecting portal hypertension, identifying characteristics of focal liver lesions, and predicting liver malignancies. Radiomics is actively used to analyse computerised lung images [27] for the timely detection of early forms of malignant tumours. By analysing quantitative information from diagnostic images that cannot be recognized or evaluated with the naked eye, it can be used to record tissue properties such as the shape and heterogeneity of their structure, their changes over time during serial imaging [25].

In oncology, the assessment of tissue heterogeneity, for example, during treatment or follow-up, is of particular interest [27, 28] as a prognostic determinant of survival and a marker of tumour aggressiveness. It has been suggested that radiomic features are directly related to genomic, transcriptomic, or proteomic characteristics of tumours [24, 27, 28]. For example, in a retrospective multicenter study [28], radiomic signatures were identified and validated in 803 patients to assess the condition of axillary lymph nodes in breast cancer. The multiple signatures, which included magnetic resonance imaging data of the tumour and lymph nodes, clinicopathological characteristics, and molecular subtypes, demonstrated a high level of prediction of lymph node status (AUC 0.93). A correlation was found between the obtained radiological features and the features of the tumour microenvironment, including immune cells and types of methylated sites.

The result of the differential diagnosis of early stages of nasopharyngeal carcinoma, which is relevant for modern oncology, was demonstrated in a recent study by L.M. Wong et al. For the screening selection of patients for malignancy among patients with benign hyperplasia, an ensemble method of processing radiomarkers was developed on magnetic resonance imaging data of 442 patients, which achieved 85% efficiency in separating pathologies ($p = 0.05$). And in the work of H. Bae et al. [30], a retrospective study of 502 patients who underwent computed tomography with contrast was conducted to differentiate between cysts, haemangiomas, and colorectal metastases to the liver. The diagnostic performance of the developed model for assessing radiological features was compared with the diagnostic performance of 4 qualified radiologists. The model demonstrated lower efficiency and specificity for haemangiomas and metastases than the doctors, but comparable diagnostic efficiency (84.36%, AUC 0.9426) for distinguishing between metastases and benign liver lesions.

However, the capabilities of new technologies are widely used not only in leading oncology clinics around the world. For example, Chinese experts [31] investigated the possibilities of preoperative differential diagnosis of tuberculous granuloma and lung adenocarcinoma, which manifest as a separate solid dense nodule in the lung. A deep learning model was built to segment the nodule on plain computed tomography images of 426 patients, of which a training cohort ($n = 123$), an internal validation cohort ($n = 121$), and an external validation cohort ($n = 182$) were identified. A comprehensive model was developed with clinical factors such as age, gender, and subjective computed tomography data (lesion size, localization, margin, multifocality, and spicules) and individualized radiomicrographs were constructed to confirm diagnostic capability. As a result, the developed diagnostic model showed 96.6%, 93.4%, and 90.6% efficiency for the training, internal validation, and external validation cohorts, respectively.

The results of the preoperative diagnosis of osteoporosis by Y.W. Jiang et al. are also optimistic [32]. In their study, a radiomarker signature based on computed tomography of 386 vertebral bodies was developed and validated for screening osteoporosis of the lumbar spine. The 3D slice module automatically extracted 1040 radiological features from the scans and created a specific signature. The sensitivity, specificity, accuracy and area under the receiver operating characteristic curve (AUC) of the Hounsfield model and the radiomic signature were calculated. The AUCs of the radiomarker and Hounsfield model were 0.96 and 0.88 in the training sample and 0.92 and 0.84 in the test sample, respectively ($p < 0.05$). Thus, the computed tomography-based radiomic signature can differentiate patients with osteoporosis before lumbar spine surgery, providing valuable information for surgical decision-making without additional costs and radiation exposure.

Important changes in medical image analysis capabilities occurred with the advent of whole slide imaging (WSI), which is the result of scanning a microscope slide with a high resolution suitable for clinical use. Specialized clinical scanners for producing such digital images became available more than 20 years ago [33, 34]. Progress in this area has improved the resolution and throughput of slide scanning, and software tools for viewing the images on a monitor screen and integrating them with medical information systems have developed [34, 35]. M.G. Hanna et al. [35] present the results of their own randomized study of the equivalence and effectiveness of the use of PCR, in which the overall diagnostic equivalence for primary diagnosis was 99.3% between the standard method and PCR. The digital method showed an increase in the time required creating a clinical report by an average of 19% per case, and no significant difference was found in terms of the researcher's personality, specialisation, or sample type.

The vast majority of publications positively characterize the use of CCD, demonstrating that their use is sufficiently appropriate in comparison with traditional light microscopy for diagnosis [36-38]. However, it is worth identifying and evaluating possible artefacts and technological risks that may affect the study result. This approach is demonstrated by P.C. Rizzo et al. [39], who present the results of a systematic literature review to analyse possible technical or diagnostic problems with the use of PCR. Of the 45 studies analysed, technical problems were reported in 15 (33%), diagnostic problems in 8 (18%), and 22 studies (49%) reported both types of problems. Technical problems included slide scanning failures, longer viewing times, and the need for higher image resolution. Diagnostic problems included cases of diagnosing dysplasia, determining the edge of invasive growth, reliable assessment of mitoses, and issues of microflora identification.

The integration of CCD technology with algorithms for detecting quantitative image data significantly increases the diagnostic capabilities of the method [40]. The software tool “HistomicsML2” of the histological pattern classifier in the detection of tumour-infiltrating lymphocytes in breast carcinoma and skin melanoma improved the recognition accuracy to 88.9%-92.4%. An important result is demonstrated by the application of a deep learning system for preliminary pretreatment marking of breast cancer [41]. When the system was applied to 44,732 BCIs from 15,187 patients with prostate cancer, basal cell carcinoma, and breast cancer metastases to the axillary lymph nodes, 65-75% of images were excluded with high confidence, while maintaining 100% diagnostic sensitivity. The impact of digital technologies on breast cancer imaging has a multifaceted effect [42], including the education of specialists with the creation of training datasets, ensuring the quality of diagnosis in terms of providing alternative viewing and the ability to archive and provide access to clinical information.

Telemedicine

The active expansion of communication networks and the increasing availability of mobile devices have prompted the rapid development of telemedicine services. Telemedicine, as the use of digital communication technologies to provide medical care to the population, has proven [43-45] to be at least equivalent to face-to-face care, improving access and reducing costs with a high level of patient satisfaction. Telemedicine can be a component of prevention, providing patients with information about their health status, monitoring chronic diseases such as diabetic retinopathy, glaucoma, and macular degeneration. The spread of ophthalmology programs has improved the quality of care for diabetic retinopathy and retinopathy of prematurity [43]. Family doctors can take advantage of a standardised approach to the assessment and diagnosis of musculoskeletal problems through telemedicine visits [45]. In oncology, telemedicine interventions include [44] remote diagnostics, remote chemotherapy monitoring, symptom management, and palliative care. Digitalisation of communication is widely used to expand access to clinical trials of cancer drugs, some of which can be used with mobile technologies. Telemonitoring of patients avoids long queues and reduces the number of hospitalizations, and electronic prescriptions reduce the number of possible errors in prescription, patient age, or dosage [43, 44].

This year's coronavirus pandemic has exacerbated the need for alternative methods of providing modern medical care. An analysis of 97614 visits by employees of 6 general and emergency medicine clinics at Stanford University [46] showed a positive attitude of stakeholders toward video consultations during the coronavirus pandemic. In 3 weeks after the almost complete transition to video visits, 53 semi-structured interviews were conducted and critical issues for further use of the program were identified. Participants emphasised the need to simplify the technology, introduce multi-party video conferencing, enable the connection of narrow specialists, and introduce trainings for doctors on virtual examination and diagnosis of patients at home.

In order to study patient characteristics that influence the choice of a video visit over a hospital visit, M.E. Reed et al [47] conducted a study of data from 1,131,722 patients who made an appointment with a primary care physician through the Kaiser Permanente Northern California patient portal. Out of more than 2.2 million appointment requests, 86% were scheduled as hospital visits, 14% as telemedicine services, and half of them as video visits. The choice of telemedicine services had a statistically significant dependence on the socio-demographic characteristics of patients: people aged 65 and older were less likely to choose telemedicine than those under 44; patients from

areas with high internet access were more likely to use video visits, and even the availability of paid parking near the clinic encouraged people to choose a telemedicine visit.

Active research is ongoing to identify and remove barriers to the widespread use of telemedicine technologies [44, 45, 48], and to assess patients' attitudes and needs. Thus, C.E. Hawley et al. [6t] in 2019-2020 assessed patients' personal needs through telephone interviews after the visit. Only 68% of patients indicated an interest in home video visits, 64% of respondents had the technical capabilities to do so, and only 42% of patients were confident that they would be able to participate. The authors divided all patients into 4 cohorts based on the principle of "interested and able," "interested and unable," "not interested and able," and "uninterested and unable" and developed special trainings for each group to overcome barriers to patient acceptance of telemedicine services. Given the cost of technical equipment and training for medical staff and patients, further research is needed to understand the scaling up of efforts and integration of telehealth visits into the population health care system [43, 45, 48].

The economic component of telemedicine services was investigated by A. Buvik et al. in a randomised controlled trial of 389 patients (559 consultations) who were referred to the University Hospital of Northern Norway for an outpatient consultation with an orthopaedist. The intervention group of 199 patients received 302 video-assisted remote consultations, and the control group of 190 patients received standard outpatient care in the hospital (257 consultations). The quality criterion was a comprehensive assessment of "quality-adjusted life years gained" (QALYs), and costs were calculated after 12 months by analysing medical records. The authors concluded that orthopaedic video consultations were cheaper than standard outpatient visits to a specialist if the total number of consultations exceeded 151 per year. With a hospital workload of 300 consultations per year, the calculated annual cost savings amounted to 18,616 euros. Thus, this work proves that, if properly organized, providing video consultations by specialists for remote facilities instead of patients coming to the center is a cost-effective measure, both from the point of view of society and healthcare institutions.

Artificial intelligence technologies have proven to be promising in many studies, but the success of clinical application depends on the conditions of patients' response to modern changes in the healthcare system. H.A. Haenssle et al. [50] conducted a patient survey to assess patients' attitudes toward artificial intelligence in melanoma diagnosis in Germany. The anonymous survey assessed patients' expectations and concerns about the use of artificial intelligence in medicine in general, as well as about various applications. About 94% of the respondents supported the idea of using artificial intelligence in clinical approaches, and 88% even expressed their willingness to anonymously provide data on their health status for the further development of telemedicine applications in medicine. As for the disadvantages of using AI-based software in medicine, patients were concerned about insufficient data protection, impersonality, and the likelihood of errors, and expected more accurate and objective diagnostics, and fewer diagnostic errors.

In a more recent study in 2021 [51], researchers assessed the potential acceptance of digitalisation by the younger generation. An anonymous online survey was conducted of the preferences and concerns of people under the age of 35 via three social networks (Facebook, LinkedIn, and Xing) regarding remote diagnosis on mobile applications for skin cancer. 66.5% of respondents expressed a positive attitude toward the use of telemedicine technologies, more so among participants living in urban areas and those who already use mobile health and fitness apps. Analysis of the responses of negative participants showed that data security, lack of trust in the app, and lack of personal interaction were the dominant problems with telemedicine use. Thus, in order to move from experimental work to clinical practice, patients of all age groups expressed demands for greater transparency and clarity of digitalisation-based tools. The critical preferences and concerns of people of all ages were similar when compared to each other and to the results.

A 2018 Cochrane systematic review [52] noted that telemedicine technologies can currently correctly identify most malignant skin lesions, but research participants' concerns about obtaining images from smartphones of sufficient quality should be taken into account. Telemedicine enables general practitioners to receive timely specialist advice on suspicious lesions of visual localisation by sending data for delayed review or interactive consultations using video conferencing to communicate between the patient, general practitioner, and specialist in real time. For the correct diagnosis of skin cancer based on photos, the average sensitivity was 94.9% and the specificity was 84.3%. For the detection of invasive melanoma or suspicious variants, the sensitivity ranged from 59% to 95% and the specificity from 30% to 93%, including the decision to refer to a specialist or excise the lesion for further diagnosis.

New perspectives for healthcare institutions and the general population arise from the interpenetration of digital wearable technology and machine learning. G.L. Farina et al. [53] studied the accuracy of automated obesity detection by deep learning using a smartphone camera. Digital lateral images of men and women were analysed in comparison with dual-energy X-ray absorptiometry. The authors developed a qualitative model for predicting fat mass based on two-dimensional digital images, which greatly simplified the practical task of identifying the obesity phenotype in adults. The gender-specific features of smartphone images and the type of obesity were significantly

correlated ($R = 0.99$, $p < 0.05$) with the results of absorptiometry. And if we combine this approach with the results of a pilot study by S.A. Alsareii et al. [54] on the creation of a new Internet of Things platform that offers ultra-reliable communication for monitoring patients' condition, we can confidently assert the enormous potential for transforming traditional healthcare systems through artificial intelligence.

Discussion

The analysed works generally reveal the positive nature of the changes caused by the widespread use of digital technologies in the field of medicine. The optimistic expectations for improving the quality of disease detection, timely diagnosis, creation of individualised treatment plans, and monitoring of prevention are generally being met in many areas of professional interest to healthcare professionals.

Eliminating many routine tasks frees up the attention of healthcare professionals and the ability to apply unique human skills. The introduction of artificial intelligence systems in healthcare facilities improves doctor-patient relationships, promotes empathy and interpersonal communication. In recent years, significant progress has been made in the development of algorithms for analysing radiographic examination methods, large amounts of publicly available image data have been collected, and artificial intelligence methods have been developed that demonstrate accuracy and efficiency equivalent to that of qualified radiologists. Smart systems in portable wearable devices based on artificial intelligence will play a key role in creating the future of healthcare.

However, some problematic issues were not covered. First of all, we are talking about one of the richest sources of clinical data - the patient's electronic medical record. The possibilities of processing natural unformalised medical records are underutilised. The unstructured text, high level of information noise, sparse and inconsistent data have not found methods for special data processing and cleaning. Inefficient technologies for keeping records should be replaced by the use of databases with standardised disease codes and harmonised vocabulary, and user-friendly software.

It's also worth noting that both researchers and practitioners are concerned about the inability to identify the criteria used by deep learning systems to achieve high performance. Several hundred criteria fed into neural networks turn into a complex system of neural output weights distributed throughout the network and cannot be analysed by humans. This creates the phenomenon of a “black box” in which we can only track input and output data, and the decision-making mechanism itself remains unclear. A shocking fact [55] was the ability of artificial intelligence to determine a patient's race based on impersonal radiological data, in which researchers could not identify any race-related features (constitutional and phenotypic features, prevalence of specific diseases, tissue density, etc.) Although the arbitrary determination of a person's race when he or she does not want it does not pose an immediate threat, the evidence that there is currently no way to control the undesirable behaviour of deep learning models requires solutions to a whole range of legal and ethical problems in the future application of artificial intelligence.

Digital technologies in the healthcare system still require public awareness, detailed testing, and further clinical trials. Before widespread implementation for direct use in clinical practice, it is necessary to ensure that computer systems are adapted to the real working conditions in medical institutions, which should include not only mechanisms for assessing accuracy and efficiency, but also rules for the safety of patients' access to the healthcare system.

Conclusions and Implications

In conclusion, the following conclusions can be drawn:

1. New technologies, including artificial intelligence algorithms, machine learning, image recognition, radiomics, and telemedicine, create the prerequisites for the development of new forms of healthcare delivery.

2. The progress of computer image recognition technologies already makes it possible to achieve diagnostic accuracy and specificity comparable to the results of experienced specialists.

3. The ability to simultaneously process large amounts of patient data using sophisticated mathematical algorithms is leading to the creation of new technologies in medicine, such as full-slide digital image visualisation or radiological signature analysis.

4. Thanks to the availability of high-quality communication and the prevalence of mobile devices, patients and doctors can interact virtually through telemedicine technologies, remotely receiving, storing, and sending clinical data.

5. The combination of telemedicine and machine learning algorithms can provide a synchronized solution to the healthcare challenges faced by modern society to ensure a healthy future for its citizens.

Declarations

Data Availability Statement

All data contained in this publication is publicly available and can be accessed via the links provided.

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Institutional Review Board Statement

D The study is a literature review and does not have grounds for review by an ethics committee.

Informed Consent Statement

The nature of the study does not require informed consent.

Conflicts of Interest

There is no evidence of a possible conflict of interest in relation to the study. Ethical issues, including plagiarism, informed consent, misconduct, data falsification, double publication, and duplication, were fully complied with.

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Innovations in medicine: modern challenges, future definitions: A narrative review

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Abstract

Background The improvement of healthcare services is one of the highest priorities for all societies worldwide. Healthcare services have shown vivid changes in the last decades due to technological advances, from examining patients and diagnosis to recently developed drugs. Although there are significant efforts to improve healthcare, humanity faces many challenges.
Aim: to study the recent medical innovations in the different aspects of healthcare services. The authors also aim to investigate the various modern challenges in medicine.
Methods: 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 strategies were used: (medical innovations) AND (artificial intelligence) AND (medical challenges). These strategies were used for searches that ended in April 2022.
Scientific novelty: Doctors used to make their own opinions in varied cases by means of limited tools. However, together with the introduction of modern technologies into the healthcare system over the previous few decades, medical practice has become increasingly dependent on technology. Medical technology is the development of instruments with the overall purpose of increasing patients' quality of life. There is much anticipation for the new tools one can create and for the outcomes they will enable, as diagnostic and treatment equipment constantly improves. Therefore, in this review, the aim is to address the tactics of the new technologies and applications in medicine.
Conclusion: Medical innovations exist in all healthcare aspects, from education and diagnosis to management. Recent technologies have demonstrated a considerable benefit in healthcare services improvement. However, a number of obstacles that both societies and individuals face are illustrated. There is a growing interest in resolving current concerns and challenges and obtaining the greatest benefits from medical breakthroughs.

Keywords: medical innovations, artificial intelligence, challenges, and healthcare.

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Introduction

Innovations in medicine can be defined as any enhancements in the individual's quality of life and the overall quality of services [1]. The healthcare services Improvement is one of the highest priorities for all societies worldwide. Healthcare services have shown vivid changes in the last decades due to recent technological advances, from examining patients and diagnosis to recently developed drugs. Recent technological innovations are also expected to keep improving the healthcare [2]. The conventional healthcare system provides medical services through an integrated approach which consists of the hospital facilities, the medical individuals, and the up-to-date equipment. Based on the country's infrastructure and individual orientation, this conventional healthcare system varies from one country to another. The recent medical technologies application may allow the general public better services, care, and flexibility [3–5]. Recent innovations allow the accessibility of information, diagnostic, and management services for the majority of people, including those in low-income countries.

Although there are significant efforts in healthcare improvement, humanity faces many challenges. These challenges are present as the recent innovations require more recently developed technologies, drugs, devices, implants, and procedures [6]. The National Audit Office Financial sustainability of the NHS reported that the cost remains the main issue in healthcare innovation. The NHS must cut costs to cover the anticipated £22 billion budget gap between patient demands and available resources [7, 8]. Due to the recent innovations, there is also an increase in the percentage of older people, usually with much comorbidity, besides; the much-rising public expectations supposing that someone needs surgery or treatment for an illness or disease. In that case, it's increasingly likely that advances in medical technology will advance the chances of a successful outcome. Medical innovations have occurred throughout history, continually advancing our ability to treat complex diseases. These include the first vaccine for smallpox in the 18th century, the development of antibiotics in the 1920s, and the world's first organ transplantation three decades later. However, the 21st century brings even more progress, with technological advances revolutionising the healthcare system. One problem with developing a product innovation is that the development time is frequently rather long. New technical and medical knowledge challenges the original invention and thus makes it necessary to adapt the product even before the innovation is marketed.

In this review the authors aim to study the recent medical innovations in the different aspects of healthcare services as well as to investigate the various modern challenges in medicine.

Research Problem

There is a significant lack in both healthcare facilities and providers. Therefore, there is rising interest in integrating new technologies in medicine. There are doubts that these medical innovations would replace physicians and make decisions. However, others suggest that these innovations have a great impact on the improvement of provided healthcare services.

Research Focus

In this review, authors focused on studying innovations in medicine and the integration of new technologies in medicine. The investigation of the roles and applications of artificial intelligence in medicine is also evaluated.

Research Questions

1. What is the current medical status?
2. What are the recent innovations in medicine?
3. What are the applications of artificial intelligence and modern technologies in the healthcare system?
4. What challenges do societies and individuals face in properly enhancing the healthcare system?

Research Aim

In this review, the authors tried to study the recent medical innovations in different medical aspects, as well as to investigate the various modern challenges in medicine.

Research Methodology

General Background

The rising demand for healthcare services has resulted in an overall medical system personnel and materials lack over time. This increased a great interest in incorporating innovative technological capabilities into medical systems in order to assist patients and clinicians in obtaining optimal and sufficient healthcare services [9]. There is evidence that AI plays a significant role in analysing medical Imaging, patients' symptoms, and investigations from electronic medical records, as well as linking these factors together to determine illness diagnosis and prognosis [10]. Despite

high attempts to enhance the healthcare, humanity face numerous challenges. These difficulties exist because current advances necessitate the use of more recently created technologies, medications, equipment, implants, and procedures. Because of recent developments, there is also a growth in the percentage of elderly persons, frequently with several comorbidities. Furthermore, the public's expectations are increasing [11]. Improving patients' quality of life remains the primary purpose of recent medical innovations.

The authors aimed to evaluate different tactics for integrating new technologies in medicine and studying the challenges in modern medicine. Thus, PubMed, Web of Science, Scopus, Embase, SpringerLink, and the Cochrane Library were searched in order to find various articles that discussed this topic. The next search strategies were used: (medical innovations) AND (artificial intelligence) AND (medical challenges). These strategies for searches ended in April 2022. Some types of publications, such as proposals, letters, procedures, and opinions were excluded. The references involve articles that were chosen as they are related to the given topic.

Statistical analysis

In this review, the results of previous trials and retrospective studies that tried to determine the best applications of modern technologies in medicine and the challenges in modern medicine were gathered and compared. So, any statistical analysis methods were not used, nevertheless conclusions are made by comparing these results.

Research Results

The authors performed the title and abstract, and then a full-text screening of these articles was effectuated in order to choose the articles related to our topic. About 624 papers concerned the recently developed technologies and the applications of these technologies in medicine. Data on artificial intelligence applications, innovations in medicine, and challenges were adequately covered in 41 articles in Figure 1.

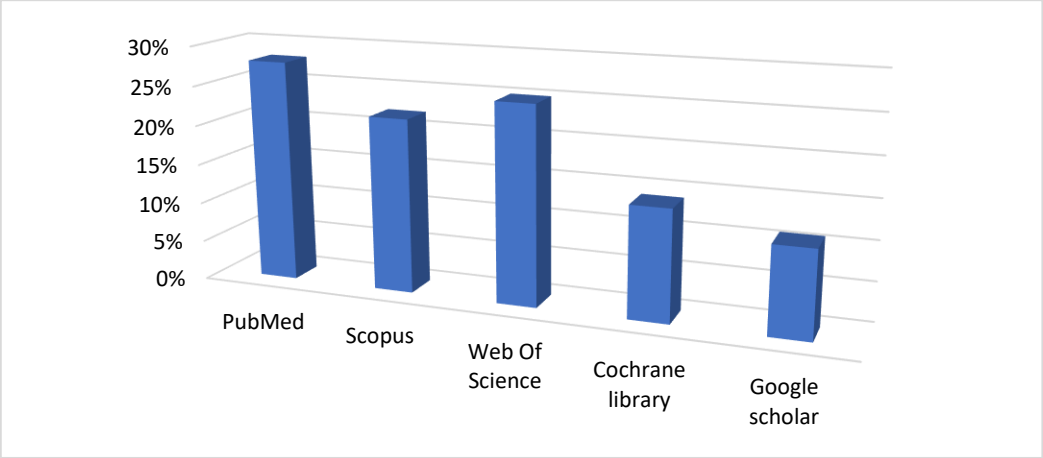

Figure 1. Showing the results of using authors' search strategy

Literature Review

In the past, doctors used to make their own decisions in various cases based on few and limited tools. However, in the last decades, with the development of modern technology implementation in the healthcare system, medical practice has become more dependent on technology utilisation [12]. The recent innovations in medicine aim not only to improve the condition of patients but also aim to increase preventive medicine by detecting symptoms and risk factors of different diseases before they are developed [11]. Medical technology is the development of instruments with the overall purpose of increasing patients' life quality. There is much anticipation for the new tools that can be created and the outcomes they could enable as diagnostic and treatment equipment constantly improves.

Innovations of diagnostic imaging techniques in medicine

Medical Imaging is a process of visualising the human body's internal organs' structure and function for clinical and therapeutic purposes, as it provides a comprehensive study of the normal and the disturbed body status in addition to treating diseases [13]. There have been intense changes in the medical imaging healthcare sciences in the last decades. Various imaging modalities showed great benefits in modern healthcare systems, such as X-ray radiography, X-ray computed tomography (CT), positron emission tomography (PET), magnetic resonance

spectroscopy (MRS), magnetic resonance imaging (MRI), endoscopy, electrical source imaging (ESI), medical photography, thermography, medical optical Imaging, single-photon emission computed tomography (SPECT), digital mammography, magnetic source imaging (MSI), tactile Imaging, and ultrasonic and electrical impedance tomography (EIT) [14]. Some modalities do not produce a diagnostic image but provide the diagnostic contribution through graphs with less accurate results than the standard imaging modalities such as electrocardiography (ECG), magnetoencephalography (MEG), and Electroencephalography (EEG). It is believed that they may be considered a form of medical Imaging but within limits.

A previous study reported that till 2010, there were about five billion investigational images had been conducted worldwide, about 3.3 billion of them were imaging that depended on ionizing radiation [15]. A previous study demonstrated that about 50% of all ionizing radiation exposure in the United States population came from various medical imaging techniques [16]. Nowadays, medical imaging modalities can diagnose almost all major medical diseases and abnormalities, including malignant, neurological, cardiovascular, surgical, and traumatic diseases but also have a crucial role in preventing, managing, and treating various abnormalities [17]. Therefore, integrating highly trained technicians who will perform the imaging technique and the experienced physician who will interpret the result is mandatory to provide the maximum benefits from these recent technologies.

Diseases medical diagnosis is considered a significant challenge in medicine. History taking and patient examination usually require a complementary modality to reach the correct diagnosis. Therefore, there is much use of the newly developed imaging techniques, which have shown great beneficial roles in helping physicians as many diseases may present with similar manifestations.

Of all mentioned modalities, a few techniques considered the newly advanced techniques in medicine, such as CT, MRI, PET scan, digital mammography, sonography, and SPECT will be described.

Computed Tomography (CT)

It is first invented in the 1969s by Hounsfield. It may also be defined as X-ray CT, which radiologists utilise to obtain clear cross-sectional images of the scanned part of the patient body. CT scanner systems have been developed over the years to enhance the obtained images (Figure 2).

Figure 2. Shows a CT scanner system that is utilised to visualise the patients' internal organs

The CT scan works by producing X-rays from different perspectives, which are finally processed by a computer to create a clear image of the diagnosed part. There are great innovations in this computed-based technology which yielded an overall improvement in the final image resolution, that in turn showed great advances in its diagnostic role [18]. The CT scan is considered an effective and reliable method for monitoring and detecting various malignancies, including bladder carcinoma, renal cell carcinoma, and cancers in different body parts [19]. Among the innovations in bone CT scan techniques are high-resolution and volumetric quantitative CT (QCT). These bone imaging modalities can investigate bone abnormalities, particularly bone malignancies and osteoporosis. Advanced CT imaging can also detect bone mineral density (BMD). CT is a safe procedure that usually does not cause harm effect. However, due to this modality's wide popularity, an increased risk of malignancy in those exposed to CT compared with control patients was demonstrated. Brain tumours and leukaemia risk were increased in children exposed to CT radiation [20]. It is well known that children are more sensitive to radiation-induced tumours than adults.

Magnetic Resonance Imaging (MRI)

MRI is one of the best non-invasive imaging modalities to visualise internal body structures and functions. It can be conducted by hardware consisting of multiple mechanical and electrical components that act together and send hydrogen ions and signals to an attached computer system in order to obtain high-resolution MR images. MRI shows a growing beneficial role in modern medical services. It is one of soft tissue's most important medical imaging modalities [21]. Many recent MRI hardware and software improvements have occurred in the last decades. Thus, scientists are looking for new MRI applications that could improve healthcare services. Unlike other imaging modalities, MRI has no risk of ionizing radiation and its adverse effects on the body. Therefore, the whole-body MRI represents one of the most prominent applications of MRI to diagnose bone metastases. MRI can detect skeletal tumours better than bone scintigraphy because there are many protons in the tumour matrix [22]. The most frequent findings made by MRI include cranial tumours, spine disorders, multiple sclerosis, stroke, musculoskeletal abnormalities, bone diseases, and vascular occlusions.

Although MRI is a powerful diagnostic and reliable test, it may alter and damage medically implanted devices, except for some stents, heart valves, and artificial joints. Furthermore, it is very expensive and takes much time for scanning and processing compared to the alternative imaging techniques. Additionally, many patients cannot tolerate the scanning and proceeding environment of MRI [23]. In addition to the diagnostic role of MRI, there is increasing therapeutic value in minimally invasive surgeries, such as treating essential tremors by thermally ablating subthalamic nuclei using MR-guided focused ultrasound surgery [24]. More innovations in MRI modality may allow for better-provided healthcare services.

Medical Ultrasound

Although it is considered to be one of the earliest developed imaging techniques since it was first used in the 1960s, it is a reliable diagnostic tool for many diseases. It gained great popularity worldwide due to its many advantages, including that it is radiation-free and has no side effects. Besides, it is much less expensive than other imaging modalities. It is also portable and easy to use [25]. Thus, it is the preferred imaging technique in children, gynaecology, and obstetrics for monitoring pregnancy and foetal health [26]. The ultrasound utilises highly frequent sound waves, which are produced by electrical signals from the ultrasound transducer. After that, the image is created by the reflected sound waves from the internal tissues as different reflected waves yield different reflected echo degrees [27]. Radiologists and special technicians can use ultrasound to visualise the liver, kidneys, urinary bladder, heart, blood vessels, and other tissues in the body.

Among the existing innovations in the field of medical imaging techniques are the 4D imaging modalities. It is an enhanced modality that utilises a combination of 4D ultrasound, 4D CT, and 4D MRI. The best techniques for diagnosing malignancies are 4D ultrasound and 4D CT. While 4D MRI is widely utilized in heart diseases [17].

Innovations and artificial intelligence (AI) in medicine

There have been rising demands for healthcare services over time which yielded an overall shortage in medical system individuals and materials. This raised the interest in integrating the recent technological facilities in the medical systems to help patients and even physicians reach optimum and sufficient healthcare services [9]. It is well known that AI has a great role in improving all aspects of healthcare services, from diagnosis to treatment. Nowadays, there is evidence that AI has a great beneficial role in analysing medical Imaging, patients' manifestations, and investigations from electronic medical records (EMRs), in addition to correlating these parameters together to reach the diagnosis and prognosis of the disease [10]. The developed smart devices provided an opportunity for healthcare providers to use medical applications and search platforms to reach any medical information at any time with its last updates. It also helped improve telehealth, providing remote healthcare services to everyone worldwide, especially in developing countries lacking specialists [28]. We believe that this technology may also provide better healthcare services in developed countries.

Although there are fears that AI will replace human existence, AI actually improves and facilitates the overall work of physicians and all healthcare staff. In 2018, Forbes studied the best medical applications of AI and concluded that AI showed the greatest benefits in analysing images, virtual assistants, robotic-assisted surgeries, and supporting clinical decisions [29]. This is consistent with other recent reports demonstrating AI applications in medical fields (Figure 3).

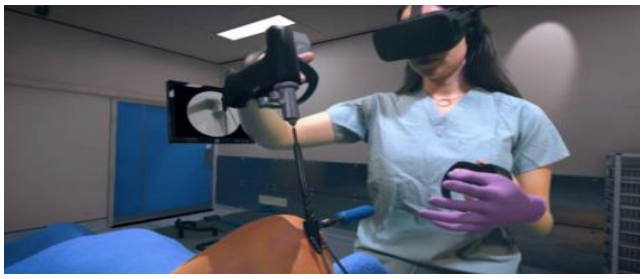

Figure 3. Showing virtual reality can help current and future surgeons enhance their surgical abilities before an actual operation [30].

Discussion

Deep learning and machine learning are parts of AI that help in solving issues in imaging applications such as medical image analysis, lesion segmentation, and computer-guided diagnosis. Furthermore, AI reports are created by enhancing the quality of images, integrating image interpretation, and biomarkers analysis [31–33]. Lung cancer is one of the most serious and common thoracic cancers. There is evidence that AI has the ability to identify benign and cancerous lesions in the lungs [31]. Deep learning algorithms learn through studying the data space and giving them better problem-solving abilities. Recently, the most commonly utilised deep learning algorithms in medical Imaging are Convolutional neural networks (CNNs) [33]. However, various deep learning algorithms showed beneficial roles in different healthcare aspects.

Cancer is considered one of the most serious diseases, responsible for one in six deaths worldwide. The malignant tumour becomes more heterogeneous on disease progression with various mixed cells. Malignancies are usually managed as a whole and homogenous disease. Thus, a deep understanding of this complexity in tumours allowed us to develop efficient treatment strategies with better outcomes [34]. Nanomedicine is a newly emerged treatment that aims to deliver traditional chemotherapy medicines in vivo, yielding better results [35, 36]. Furthermore, the targeted therapy is another cancer treatment modality that targets a specific area in the tumour, such as intracellular organelles or the tumour vasculature [37]. Moreover, gene therapy depends on modifying gene expression, triggering cancer cells' apoptosis. Among the contributing innovative therapeutic techniques are pathomics and radionics [38–40]. They can aid in collecting data, developing new therapeutic techniques, predicting the treatment response, and the overall disease prognosis.

Volosovets et al. studied the current challenges in the Ukrainian healthcare system from the official statistical data from 2009-2020 [41]. They found that there are many challenges, such as a lack of physicians and the high costs of medical services. They suggested that more medical education and increasing the number of medical students may help replenish the existing deficit of medical personnel. Additionally, they suggested more changes in contributing to the new activities and technologies in the healthcare systems.

There are various medical innovations in all aspects, from education and diagnosis to management. Recent technologies have shown a significant beneficial role in improving healthcare services. However, several challenges facing both societies and individuals were demonstrated. There is a rising interest in solving the current issues and challenges in addition to getting the maximum benefits from innovations in medicine. The development, adoption, and diffusion of innovation in health care cannot be taken for granted. The vast majority of innovations—great ideas with very good intentions—will never find their way into the healthcare market, even if they have the potential to meet people's needs. Profit certainly plays a role, but using the right tools and having the knowledge of innovations are even more important. The process from the original idea to the establishment of the innovation as the new standard solution requires professional management, i.e., proper planning, thorough organisation, appropriate staffing, constant motivation, and many forms of control and synchronisation. Innovations in health care can be minor (such as a new wrapping for sterilising) or remarkable (such as a completely new paradigm of medicine and a shift in human understanding of health and disease). The existing world is the result of innovation processes of the past—and the future world will be the consequence of today's innovation processes. Whether this future brings a better quality of life, more efficient health care provision, and equity among stakeholders depends a lot on the inventions are made today, the adoption process, and current diffusion. What humanity expects in the near future is definitely an integrated and patient-centric healthcare system. Technologies such as big data, AI, IoT, and augmented & virtual reality will increasingly make their way into this field; this and other environmental variables will pave the way for reconfiguring ecosystems involving new stakeholders. Hospitals will be rethought as a function of an increasingly tangible switch from a treatment regime to one that will allow people to cope with certain pathologies (mostly chronic) directly in their own homes. All of this necessarily requires that healthcare professionals acquire new

knowledge and skills and those healthcare systems worldwide make a collaborative effort, as suggested by the Covid crisis in such a way that geographical distances are shortened and inequities in the use of healthcare services are reduced.

Conclusions and Implications

1. There is a global interest in integrating new technologies in medicine.
2. Preparing the public, healthcare professionals and policy decision-makers for the future of medicine is critical.
3. The Med Tech field needs to work as a community proclaiming their new high-quality approaches and integrating them across organ sectors.
4. Newly developed technologies have a beneficial role in developing overall healthcare services.
5. Mobile medical technology is expanding with multiple diagnostic and monitoring platforms using mobile app systems, which can require new ways of approaching data analytics.
6. AI has several applications in all medical fields that have a significant impact on the current healthcare systems.
7. We are facing challenges in the development of these enhancements.
8. It is necessary to provide potential opportunities for new technologies in order to reach an improved comprehensive medical service.
9. Technology and innovations in medicine aim to globally help all patients, providing evidence for particular conditions that need to be personally considered, involving the patient's decision while treating, forecasting, and preventing disease.
10. Policymakers must integrate medical approaches into national strategies in order to improve the healthcare.

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Risks of anaesthetic management during laparoscopic interventions on the abdominal aorta and its branches

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Abstract

Aims: The main goal of this study is to draw attention to the dangers of anaesthetic management during laparoscopic procedures on the abdominal aorta and its branches.

Methodology: In this study, the risks of anaesthetic management during laparoscopic interventions on the abdominal aorta and its branches were determined by a systematic search use. The most recent studies in Scopus, PubMed, and google scholar databases. The search terms used were: [Risk OR adverse effect OR side effects] AND [Anaesthesia OR Anaesthetic management] AND [laparoscopic intervention or laparoscopy] AND [abdominal aorta OR abdominal aortic aneurysms] were evaluated.

Results: 1070 articles using electronic databases were first collected. After a deep search, 238 articles were selected and given to the writers for additional evaluations. A thorough brainstorming session that resulted in the selection of 12 relevant papers for the evaluation was conducted. Abdominal aortic aneurysms (AAAs) that is affected by age necessitate surgical treatment. For AAA patients, laparoscopic surgery has become a vital procedure with a number of advantages. Laparoscopic surgery has become a standard medical procedure because it reduces tissue trauma and provides significant advantages. The administration of anaesthesia in patients having laparoscopic surgery, however, is crucial and demands special attention. Despite the rarity of absolute contraindications, the anaesthetist must carefully choose the patients who may undergo such procedures and must constantly be prepared for intraoperative issues. The pain experienced by patients having laparoscopic operations, such as appendectomy, is likely to be understated, so small incisions do not always imply reduced pain levels.

Scientific Novelty: This is the first systematic review that highlights anaesthetic management during laparoscopic interventions on the abdominal aorta and its branches risks.

Conclusion: In extended laparoscopic surgery, general anaesthesia and epidural analgesia can be used together with the advantage of reduced postoperative pain severity thanks to patient-controlled spinal anaesthesia.

Keywords: Spinal anaesthesia, abdominal aortic aneurysms, critical assessment tools

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Introduction

Laparoscopic surgery is one of the most important tools for diagnosis and treatment in the current medical era. This has been the industry norm ever since Phillipe Mouret effectively completed the first laparoscopic

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cholecystectomy in 1987 [1]. Less discomfort, quicker hospital stays, early mobilisation, and minimal damaging are all advantages of minimal access methods that have led to an increase in their use [2]. Pneumoperitoneum is needed for sufficient visualisation and operative handling during this minimally invasive treatment. The intra-abdominal pressure and the gas use both affect systemic changes, particularly cardiovascular changes. The primary concerns during laparoscopic surgery are the cardiovascular consequences of pneumoperitoneum, venous gas embolism, systemic carbon dioxide absorption, accidentally damaging intra-abdominal structures, and patient positioning [3, 4]. During the laparoscopy, the surgeon has a limited range of movement from a tiny invasion hole and has difficulty in feeling tissue, hence unable to judge the force needs to be applied.

The pathophysiologic changes brought on by the formation of the pneumoperitoneum and the necessary positioning of the patient confounds anaesthesia in laparoscopic operations. The length of the procedure is typically lengthier, the possibility of visceral damage, and the difficulty of estimating the amount of blood loss when haemorrhage happens all this contribute to the procedure's potential for high risk. To be ready to avoid, identify, and treat any potential changes that might take place during the operation, the anaesthesiologist needs to have a thorough knowledge of the pathophysiological effects caused by the pneumoperitoneum.

Research Problem

Laparoscopy for general surgery has advantages such as decreased intraoperative bleeding, decreased postoperative pulmonary problems, decreased postoperative wound infections, less metabolic disturbance, and better postoperative respiratory function. Additionally, it resulted in faster returns to regular activities, shorter stays in hospitals, and lower total medical expenses [5]. Anaesthesia during laparoscopy has become more logistically challenging in recent years as improved laparoscopic surgery has targeted elderly and sicker patients. Laparoscopy was developed as a secure, straightforward operation that could be done as an outpatient procedure, so it demands great care regarding the anaesthetic method. On the other hand, it can impair the patients' cardiovascular and respiratory systems. In order to provide the best anaesthetic treatment and enable early detection and complications reduction, laparoscopic surgery provides the anaesthesiologist with a number of new challenges.

Research Focus

The aim of anaesthetic management for patients undergoing laparoscopic surgery should be to facilitate physiological changes during surgery with minimal influence on the body's vital systems and rapid anaesthesia recovery with insignificant aftertaste. These changes may all be detected by keeping an eye on the electrocardiogram (EKG), the non-invasive arterial pressure (NIBP), the pulse oximeter (SpO2), the airway pressure, the et-CO2 concentration, the peripheral nerve stimuli, and body temperature. When a patient's cardiopulmonary function is impaired, it's also important monitoring their urinary production. Additionally, the urinary procedure reduces the possibility of bladder damage during port placement. Atropine must be used with caution because it raises the chance of tachyarrhythmia while also preventing vagal stimulated bradyarrhythmia [6]. There is a need of research to determine the risks of anaesthetic management during laparoscopic interventions on the abdominal aorta and its branches.

Research Aim and Research Questions

The main goal of this study is to draw attention to the dangers of anaesthesia used during laparoscopic procedures on the abdominal aorta and its branches. The following research questions have been address:

1. Does laparoscopic interventions poses any complications on the abdominal aorta and its branches?
2. Do pneumoperitoneum and the positioning of the patient confound anaesthesia in laparoscopic operations?
3. What are the risks of anaesthetic management during laparoscopic surgery?

Literature Review

The night before operation, doctors may give benzodiazepines or other benzodiazepine-like hypnotics to anxious patients. Ondensetron use is advised preoperatively because postoperative nausea and vomiting (PONV) is a laparoscopic surgical risk that is anticipated. The preferred anaesthetic methods for abdominal laparoscopic surgery include general anaesthesia with muscle paralysis, tracheal intubation, intermittent positive pressure breathing (IPPV) with small tidal volume, and addition of a positive end-expiratory pressure (PEEP) of 5 cms of water [7]. A more recent advancement in the anaesthetic technique is the use of a laryngeal mask airway (LMA), which maintains the patient's spontaneous breathing. Ryle's tube aspiration should be used to compress the stomach during trocar insertion to lessen the possibility of gastric injury. It is controversial whether nitrous oxide should be used during laparoscopic surgery since it might result in intestinal distension [8]. Because it has fewer symptoms that can cause arrhythmia and cardiac depression, isoflurane is the favoured volatile anaesthetic drug. For casual gynaecological laparoscopic operations, epidural anaesthesia has been used to decrease problems and speed up the post-anaesthesia healing process [9]. Some studies claim that ventilation with a large tidal volume of 12 to 15 ml/kg stops the progression of

alveolar atelectasis and hypoxemia and allows for more effective alveolar ventilation and carbon dioxide elimination [10], but other studies back ventilation with a moderate tidal volume and the addition of PEEP. The difference between PaCO2 and PECO2 can be used to assess the ventilation's effectiveness. In healthy individuals undergoing general anaesthesia, it ranges from 2 to 9 mmHg [11]; however, the gradient between PECO2 and PaCO2 may become elevated and unstable in patients with impaired cardiopulmonary function. Therefore, arterial blood gas measurement may be required to directly estimate PaCO2 in order to identify hypercarbia [12]. A PECO2 sensor is useful for venous gas embolism early identification as well [13]. In anaesthetised patients getting IPPV, It's important to check the airway pressure on a frequent basis because a high airway pressure alert can help identify an excessive increase of intra-abdominal pressure [14]. The literature review provides information about the previous studies concerning the risk during the laparoscopy with varying results. In the present systematic review focused on the risks of anaesthetic management during laparoscopic interventions on the abdominal aorta and its branches. This will provide information in managing these risks for the laparoscopic surgery.

Methodology

General Background

The studies included in this review used a range of study designs, many of them did not adhere to traditional procedures for data collection and theoretical tenets. One carried out keyword searches in the Scopus, PubMed, and Google Scholar databases to find pertinent papers. The search terms used were: [Risk OR adverse effect OR side effects] AND [Anesthesia OR Anesthetic management] AND [laparoscopic intervention or laparoscopy] AND [abdominal aorta OR abdominal aortic aneurysms]. These keywords were intended to help locating the papers that addressed the subject of our research. We looked for and selected peer-reviewed English-language research articles from these keyword searches. The relevancy of the titles, abstracts, and keywords was checked by two independent reviewers. Publications having titles or abstracts that complied with the requirements for this systematic review were chosen for a more thorough examination. Before adding the article to the research, the whole text of each article was read in case there was any ambiguity. Pre-prints were not included since we were unable to assess their reliability because the scientific community had not yet publicly recognised them through the peer-review process. Articles that omitted any of the aforementioned details were not included in this study (Table 1).

Table 1. Inclusion and exclusion criteria for studies

Inclusion criteria	Exclusion criteria
Studies on risks of anaesthetic management during laparoscopic interventions	Anything not including the listed topic
Peer reviewed scientific articles	Anything other than peer-reviewed articles and literature
English language research	Publications in languages other than English

Author's development

Data Analysis

The current study conforms to all advised research ethical standards. Since this study was a review of the findings of other previously published articles that were accessible to the public, the Research Ethics Committee did not formally approve it.

Results

A number of standards were utilised for the article eligibility, as listed in Table 1, in accordance with the PRISMA principles and critical assessment tools to guarantee the calibre and consistency of the identified articles. The authors first retrieved 1070 papers for use in electronic databases. These publications were then compared to the study's goals, and any that didn't fit the bill were disregarded. 238 publications were chosen after further screening and dispersed to the authors for additional evaluations. A comprehensive brainstorming session by the authors led to the inclusion of 12 pertinent articles in the review (Figure 1).

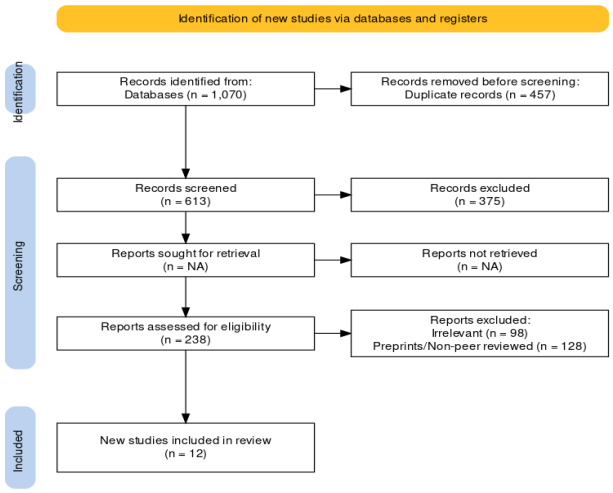

Figure 1. **The PRISMA flow chart of the literature selection for the systematic literature review (author's development)**

Discussion

The present study focuses on the risks of anaesthetic management during laparoscopy. The 13th most common cause of mortality in the US is abdominal aortic aneurysms (AAAs) [15] and each year, 40,000 individuals have elective AAA repair [16]. With an average age of 70, AAA primarily affects the aged, and its frequency rises as people mature. Surgical treatment options rely on the site and severity of the illness and may include open repair or endovascular stenting. Laparoscopic surgery, as opposed to open surgery, carries a 0.3% to 1.8% reduced chance of cardiovascular morbidity and death [17]. As a result, laparoscopic surgery is commonly performed on high-risk individuals. However, compared to low intra-abdominal pressure, high intra-abdominal pressure brought on by CO2 insufflation in these high-risk individuals is linked with more changes in hemodynamic parameters, raising the risk of cardiovascular problems [18]. In current study, we systematically reviewed the risks of anaesthetic management during laparoscopy.

An increase in intra-abdominal pressure causes the venous blood return to be mechanically impaired, which causes the preload to decrease and the afterload to rise. The systemic vascular resistance (SVR), mean arterial pressure (MAP), and heart output will all rise [17]. The top portion of the body is typically most affected by high MAP. A further reduction in blood flow downstream to the coarctation may result from a rise in the SVR caused by the development of pneumoperitoneum, along with a decline in the stroke volume, cardiac, and ejection velocity parameters. Laparoscopic procedures benefit from low-pressure pneumoperitoneum because it reduces the negative cardiovascular impacts of CO2 insufflation [18]. The results of the given systematic review are in line with the previous studies highlighting the risks during laparoscopy.

To reduce circulatory alterations during pneumoperitoneum, intra-abdominal pressure should be kept below 12 mmHg [19, 20]. It is thought that sufficient tissue perfusion requires a MAP 60 mmHg. Laparoscopy surgery had advantages such as decreased intraoperative haemorrhage, decreased postoperative pulmonary problems, decreased postoperative wound infections, decreased metabolic disruption, and better postoperative respiratory function. It also produced better cosmetic results, allowed for a quicker return to normal activities, and reduced hospital stays, which reduced overall medical costs [5]. In current study, the findings also suggested the advantages and disadvantages as reported previously.

Laparoscopic procedures have several advantages and disadvantages as presented in Table 2.

Table 2. **Laparoscopic surgery advantages and disadvantages in terms of surgery**

Advantage	**Disadvantage**
Intraoperative:	
Less blood and coagulation factor transfusions are necessary due to decreased blood loss [21] Reduced tissue trauma An image of the whole abdominal cavity	Extended operational period A higher price Technique is more difficult and there is no tactile feedback Surgery to treat bleeding issues may take longer than expected Some surgical devices are not functional
Postoperative:	

Improved anaesthetic outcomes Less pain and less need for analgesia Longer recovery times with preserved lung function Lower incidence of wound infections Reduced hospitalisation	Tissue damage and nerve damage brought on by placement and lengthy operations

Source: [22-26]

Surgery needs and physiological changes during the surgery process must be taken into account when managing anaesthesia for patients having laparoscopic surgery. The most common way to conduct laparoscopic surgery is under general anaesthetic with positive pressure ventilation and a cuffed endotracheal tube, which provides the over minute respiration and PaCO2 control. Due to the elevated danger of aspiration and ventilation issues brought on by the greater airway pressures necessary during pneumoperitoneum, the use of the laryngeal mask airway (LMA) during laparoscopic abdominal surgery is still debatable [27]. In the present study one focused on the risk of the anaesthetic management during the laparoscopy.

The objective of anaesthesia is to maintain greater arterial blood pressure (ABP) proximally, maintaining ABP distal to coarctation at 60 mmHg or higher. Other accompanying diseases like left ventricle enlargement, intracranial aneurysm and ischemic heart disease, may change the condition management [28]. The primary issues with laparoscopy are higher intra-abdominal pressures, patient positioning, and carbon dioxide insufflations. Pneumoperitoneum should be started with reduced gas flow and intra-abdominal pressures should be kept as low as possible to reduce hemodynamic alterations [29]. The current study highlight that anaesthesia poses risks during laparoscopy management.

The minimum pressure required to cause minor hemodynamic alterations during pneumoperitoneum is 12 mmHg. The preload decreases when the intra-abdominal pressure rises, as a consequence the afterload, the systemic vascular resistance and the intra-abdominal pressure rise [30]. The upper part of the body is typically most affected by high ABP. The development of pneumoperitoneum increases total peripheral resistance and decreases the heart ejection velocity, as well as stroke volume parameters [31, 32]. Further reduction in blood flow downstream to the coarctation may result from these alterations. To keep the blood pressure within safe ranges, intrusive ABP tracking is used. It's crucial to choose the right location for ABP tracking. It is wise to assess ABP both proximally and distally to the coarctation in order to gauge the body's circulation. With the exception of brief gynaecological operations, local or regional methods have not been recommended as the only type of anaesthesia for laparoscopic abdominal treatments. In order to eliminate the pain of surgical stimulus, which could result in myocardial depression and exacerbate the effects of the pneumoperitoneum, a strong block (T2-T4 level) is necessary [4]. Additional drawbacks include the need for more breaths to be taken in, how the patient is positioned, and diaphragmatic discomfort, which may not be relieved in a conscious patient by spinal anaesthetic alone [33].

The patient's circulatory system state is influenced by a wide range of laparoscopic surgery-related variables. The most notable example of this is the rise in intraabdominal pressure (IAP) brought on by the patient's posture and CO2 expansion. As pneumoperitoneum develops, the IAP gradually increases, increasing strain on the splanchnic vessels. In the initial stages of the laparoscopic operation, this causes an increase in loading and a subsequent rise in blood pressure. Catecholamines may be released in reaction to pain and the neuro-humoral response to peritoneal straining, which can cause serious increases in blood pressure and tachyarrhythmia [34]. Vein failure is a possibility if IAP is greater than IV pressure in the splanchnic veins; this effect is then reversed to increase inferior vena cava compression. Hemodynamic instability may be exacerbated by co-morbidities, surgical handling, anaesthetic-induced vasodilation, release of prostaglandins and hemodynamic instability. Changes in the patient's posture are also essential. For instance, cholecystectomy surgery involves anti-Trendelenburg posture, which may result in a reduction in the Cardiac Index (CI) because of a reduced venous return from the lower body. Trendelenburg posture is frequently required for procedures in the lower abdomen quadrants. Venous return rises as a result of the elevated lower torso, which in turn elevates CI, central venous pressure (CVP), and intracranial pressure (ICP) [34, 35]. The results of this study showed that the patient's circulatory system state is important during the laparoscopy.

The anaesthetist should be ready for either severe hypertension or severe hypotension depending on the stage and method of the operation. IAP should be closely monitored, with a goal of ≤15 mmHg [36]. Postoperative lung function is also impacted by intraoperative lung airflow compromise and atelectasis development [37]. These findings are in accordance to our research hypothesis.

Patients who have had laparoscopic surgery have both the forced expiratory volume and vital capacity [38]. The circulation of abdominal organs like the kidney and liver will be compromised as IAP increases and surpasses the abdominal arteries' arterial pressure, and venous outflow will be decreased. Reduced glomerular filtration results

from decreased urine output and retained creatine, as well as decreased renal blood flow. Optimising the venous capacity can lessen the impact of this [39]. The findings of this study are in line with our research question.

The anaesthetist should monitor the patient's renal function, perioperative diuresis, and intravascular volume condition. Hepatic failure and an increase in liver enzymes can be observed if the liver's blood flow or venous outflow are compromised [40]. These side effects are typically self-limited and have no morbidity in individuals with adequate liver function [41]. The anaesthetist should be concerned about liver function if there is a history of liver dysfunction or if the increase in IAP is markedly protracted.

As with pneumoperitoneum, CO2 in the abdominal region will eventually be reabsorbed into the bloodstream. IAP, the site of CO2 administration, and the stage of the process all affect abdominal CO2 resorption. There is proof that pleural CO2 will not be resorbed as quickly as extra-peritoneal insufflates CO2, which is used in laparoscopic circumcision [42]. CO2 resorption will rise at the start of the operation with the commencement of pneumoperitoneum, reach a stable state, and may temporarily rise again after the release of pneumoperitoneum at the end of the surgery because of the increase in venous return with lowering IAP. After being reabsorbed, the CO2 is then transported to the lungs, where it will be expelled with the CO2 produced by normal metabolism. Because CO2 partial pressure impacts acid-base balance, breathing needs to be controlled to prevent hypercapnia and acidosis. To meet the respiratory demand brought on by a rise in CO2 resorption in the pneumoperitoneum, minute respiration must be raised by up to 15% [43]. The findings of our review also suggested that anaesthetic management should be done through restoration of respiratory function.

It has been proven that using a valve-less trocar by the surgeons during robot-assisted radical cystectomy enhances respiratory mechanics. It has also been suggested that this technique may reduce the need for extended pneumoperitoneum [44]. The results of this systematic review are in line with the findings of this study.

The doctors should be requested to lower IAP or temporarily halt the CO2 supply if ventilator adjustment is not an option. Otherwise, hypoventilation causes acidity and hypercapnia. Acidosis and elevated pCO2 cause the cerebral arteries to dilate, which is followed by a rise in cerebral blood flow and ICP. In individuals with right heart failure, acidosis can cause pulmonary vasoconstriction, which raises pulmonary vascular resistance and increases the right-left shunt, all of which can result in cardiac decompensation. Therefore, it's crucial to continuously check the patient's end-tidal pCO2 (petCO2), acid-base balance, and gas exchange.

The danger of postoperative nausea and vomiting (PONV) and anaesthesia gas emissions in the operating room are both decreased when propofol is used in total intravenous anaesthesia (TIVA) [45]. In addition, propofol might prevent an increase in intraocular pressure (IOP) after Trendelenburg posture and pneumoperitoneum, in contrast to sevoflurane [26, 45]. While inhalational anaesthesia has been controversially discussed even in cardiac surgery, balanced anaesthesia provides the benefits of better monitoring and perhaps safer anaesthetic supply if venous access is not visible, such as if arms are linked to the body throughout the treatment, [26, 46]. Additionally, compared to propofol, the suppression of spine responses is more evident when using volatile anaesthetics like sevoflurane [47, 48].

In extended laparoscopic surgery, general anaesthesia and epidural analgesia can be mixed with the advantage of reduced postoperative pain severity thanks to patient-controlled spinal anaesthesia (PCEA). There is evidence that individuals undergoing upper abdominal laparoscopic surgery who have pulmonary risk factors benefit even more from thoracic epidural analgesia [49]. For every patient, the advantages of spinal anaesthesia may not, however, exceed the risks. As a result, thorough individual benefit-to-risk analysis is required. To enable sufficient ventilation when IAP is raised in a pneumoperitoneum with CO2 and extreme placement, the airway control is crucial. Higher ventilation rates and aspiration avoidance are both feasible here. Even though intubation is the gold standard, the use of second generation supraglottic airway devices can be investigated in some circumstances, such as lower abdominal and pelvic surgeries. Because they provide an optimal fit and the option to insert a stomach tube, these devices may be able to provide safe breathing in laparoscopic procedures even in obese individuals [50]. There is evidence that when laryngeal masks are used instead of endotracheal intubation, PONV and postoperative throat pain diminish, as well as hemodynamic alterations that occur during endotracheal intubation are prevented [51, 52]. It has been established that pressure-controlled breathing and muscle inhibition are the best methods for ensuring adequate oxygenation and lung protection [53]. There is some evidence to suggest that deep neuromuscular blocking, as opposed to mild neuromuscular block, can enhance surgical conditions and potentially enable for the use of reduced IAP [54]. The question of whether this technique is usually advised, should only be used in certain procedures, or even be reserved for challenging surgical circumstances, is still up for debate [55, 56]. Controlling and treating atelectasis development calls for careful lung recruitment strategies and adjustment to an adequate positive end-expiratory pressure (PEEP) [57]. Therefore, careful consideration of anaesthetic management during laparoscopic procedures should be made depending on the type of operation and the health of the patient.

Conclusions and Implications

1. Abdominal aortic aneurysms (AAAs) are most common in elderly people and must be treated surgically.
2. The laparoscopic procedure has gained popularity and offers AAA patients a number of advantages.
3. The laparoscopic surgery provides significant advantages through decreased tissue trauma. However, the management of anaesthesia in patients having laparoscopic surgery is vital and necessitates special attention.
4. Although absolute contraindications are uncommon, the anaesthetist must carefully choose which patients can endure such operations and must always be ready for intraoperative problems. The pain experienced by patients having laparoscopic operations, such as appendectomy, is likely to be understated, so small incisions do not always imply reduced pain levels.
5. Total intravenous anaesthesia with propofol lowers the risk of postoperative sickness and vomiting and lessens anaesthesia gas emissions in the operating room and surrounding areas.
6. In order to reduce subsequent pain severity, general anaesthesia and patient-controlled epidural anaesthesia can be used during intensive laparoscopic surgery.
7. It is also possible to accomplish the anaesthetic management through restoration of respiratory function.
8. The risks of anaesthesia should always be considered in laparoscopic surgeries in order to avoid complications during and after the surgery.

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Analysis of the state of medicine in Pakistan: challenges and future prospects

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Abstract

Aims: This article examines the condition of medicine in Pakistan utilising existing scientific articles, reports, and other published information in order to describe the position of the country regarding medication quality and the presence of deprived and/or false pharmaceutical preparations.

Methodology: In this study, studies concerned with the condition of medicine in Pakistan have been systematically searched. The most sustainable recent studies on the condition of medicine in Pakistan in PubMed, Medline, the Cochrane library, EmBase, and Google Scholar were evaluated for this systematic review. The search criteria were [Medicine or drug] AND [analysis] AND [Pakistan]. To guarantee the caliber and consistency of the selected articles, many criteria were utilised for article eligibility, in accordance with the PRISMA principles and critical assessment tools.

Results: The authors first retrieved 750 papers for use in electronic databases. These publications were then once again compared to the study's goals, and any that didn't fit the bill were disregarded. After further screening 40 publications were chosen and dispersed to the authors for additional evaluations. The authors' detailed brainstorming session resulted in the inclusion of 18 pertinent papers in the review.

Scientific Novelty: This is the first systematic review performed in Pakistan in order to highlight the state of medicine.

Conclusion: The research suggests that to effectively regulate substandard and counterfeit medication in Pakistan, regulatory procedures for facility inspections and Good Manufacturing Practices (GMP) assessments, analytical laboratories, and capacity building, all need to be strengthened. The material that is currently available cannot support the claim that 40–50% of Pakistan's medications are of low quality. The primary causes of the subpar services provided by community pharmacies include a lack of competent personnel, a lack of advice, and a lack of professionalism on the part of the dispensers, as well as the vagueness of rules and how they are applied.

Keywords: medication quality, PRISMA, systematic review, good manufacturing practices.

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Introduction

Due to the country's poor financial, economic, and environmental conditions, health issues in Pakistan are on the rise every day, and treatment options are limited [1]. The main cause of poor health conditions is the poverty. Past researchers have established a clear causal connection between poverty and health [2]. Citizens must be well-educated, benefit from a robust economy, have access to the newest technologies, and most importantly, have a constant and established contact with medical specialists in order to combat numerous diseases and health issues [3]. People in Pakistan shy away from patronising state-run hospitals because of their "poor quality" and "unreliability." [4]. The WHO states that in order to reach the greatest level of human health, the availability of critical medications that are safe, effective, and of high quality is important [5]. However, reports of regular drug lacks from high-income, middle-income, and low-income nations have been made. [6]. According to the WHO, about 2 billion people have no access to basic medications [7] which results in subpar medical care and expensive financial consequences. In order to satisfy patient and public health demands, the WHO defined medication deficit as "the supply of medicines, health products, and vaccines identified as essential by the health system is considered to be insufficient" [8]. A lack of medicines according to the US Food and Drug Administration (FDA), is a period of time when demand or projected demand for the medication outweighs supply [9]. The lack of access to medicines is not a recent problem, but its scope and severity have grown in recent years [10]. According to the American Society of Health-System Pharmacists (ASHP), by the end of 2017, 146 pharmaceuticals were in limited supply (this number rose to 224 by the end of June 2018) [11]. According to a Canadian research from 2018, there were yearly shortages of about 1000 medicines [12].

Research Problem

Since a very long time ago, Pakistan has been addressing the threat posed by subpar medications. The Drugs (Generic Names) Act (XXIV of 1972), which established the generic policy, was revoked in 1975 as a result of the suspension of 38 pharmaceutical companies for creating inferior medications [13]. The Drugs Act of 1976 established fines (100,000–100,000 Pakistan Rupees, or $707–7067 USD) and legal penalties (five–ten years in jail) to prohibit drug counterfeiting as well as the sale and manufacture of medications without a licence and market authorisation. Along with post-earthquake rescue activities, the WHO established a network for the distribution of medications in 2005 with the intention of identifying and resolving quality and supply problems in the affected areas as soon as possible [14]. Several organisations nationwide implemented the WHO prequalification programme [15], this improves the delivery of medications of the highest calibre. In a local study, there was no discernible difference in the amount of time needed for smear conversion between locally produced, multiple drug resistant tuberculosis drugs purchased through the medicine prequalification programme and the 15-20% more expensive, internationally quality assured medicines [16]. The lack of resources is a major factor in weak regulatory controls, particularly when it comes to the analytical testing of medications. To ensure the population's continuous access to high-quality drugs, Pakistani regulators and researchers need to be informed about the affordable technologies and strategies associated to establishing cost-effective policies. This synthesis can act as a catalyst for regulatory system change in Pakistan and make it simpler to provide safe and efficient pharmaceuticals to the general public.

Research Focus

In Pakistan, 40–50% is the most often cited estimate for the incidence of subpar medications [17]. However, this statistic has come under fire for lacking factual information in another publication on the overall quality of Pakistani drugs [18]. Regarding the failure rates reported by Pakistan's public sector Drug Testing Laboratories (DTLs), little information is known. Evidence-based policies are essential for making the best technological decisions and for building the technical expertise needed to look into problems like adulterants, pharmaceutical contaminants, and performance difficulties. To provide such evidences, researchers with experience in policy, regulation, and analytical methods collaborate closely. The prevalence of low-quality medications is well-documented in international literature, mostly from sub-Saharan Africa, where the accessibility of basic field data has enhanced awareness of the issue and inspired resources to devise remedies through internal and external initiatives. In Pakistan, the provincial governments are in charge of distribution and sales while the federal government manages licensing, production, registration, pricing, and imports and exports of pharmaceuticals [19]. International analysts consider this decentralised regulatory control as a fundamental weakness in the system [20]; the issue worsened when the 18th amendment to the Pakistani constitution moved drug regulating power from the federal government to the provinces [21]. Provinces through the Council of Common Interest eventually issued a "no objection" certificate, reversing the judgment. Along with drug control, the Higher Education Commission is another entity that was subject to government regulation [22].

Research Aim and Research Questions

This review's primary objective is to analyse the state of medicine in Pakistan using data that is currently available in reports, scientific publications, and other published sources that can be helpful in describing the situation of the country with the regard to the quality of medicines and the prevalence of substandard and/or counterfeit medical products. The challenges and future prospects of state of Medicine in Pakistan will be highlighted.

Research Methodology

General Background

This study involves a systematic search for studies related to state of medicine in Pakistan. For this systematic review, PubMed, Medline, EmBase, the Cochrane library, and Google Scholar articles were searched for the most current research on state of medicine in Pakistan. The terms [Medicine or drug] AND [analysis] AND [Pakistan] were used as search criteria. Searches were restricted to English language articles only. The relevancy of the titles, abstracts, and keywords was checked by two independent reviewers. Publications having titles or abstracts that complied with the requirements for this systematic review were chosen for a more thorough examination. Before adding the article in the research, the whole text of each article was read in case there was any ambiguity. Articles were chosen for evaluation if they had described the rational drug use in Pakistan, the contributing reasons to it, and the results of that rational usage. Articles that failed to include any of the aforementioned points were excluded from this research (Table 1).

Table 1. Inclusion and exclusion criteria for studies

Inclusion criteria	Exclusion criteria
Studies on state of medicine or drug in Pakistan	Anything not including the listed topic
Peer reviewed scientific articles	Anything other than peer-reviewed articles and literature
English language research	Publications in languages other than English

Author's development

Data Analysis

The current study conforms to all advised research ethical standards. The Research Ethics Committee did not formally authorise this study since it was a review of the findings of other previously published publications that were available to the public.

Results

A number of standards were utilised for the article's eligibility, as listed in Table 1, in accordance with the PRISMA principles and critical assessment tools to guarantee the calibre and consistency of the identified articles. The authors first retrieved 750 papers for use in electronic databases. These publications were then once again compared to the study's goals, and any that didn't fit the bill were disregarded. 40 publications were chosen after further screening and dispersed to the authors for additional evaluations. A comprehensive brainstorming session by the authors led to the inclusion of 18 pertinent articles in the review (Figure 1).

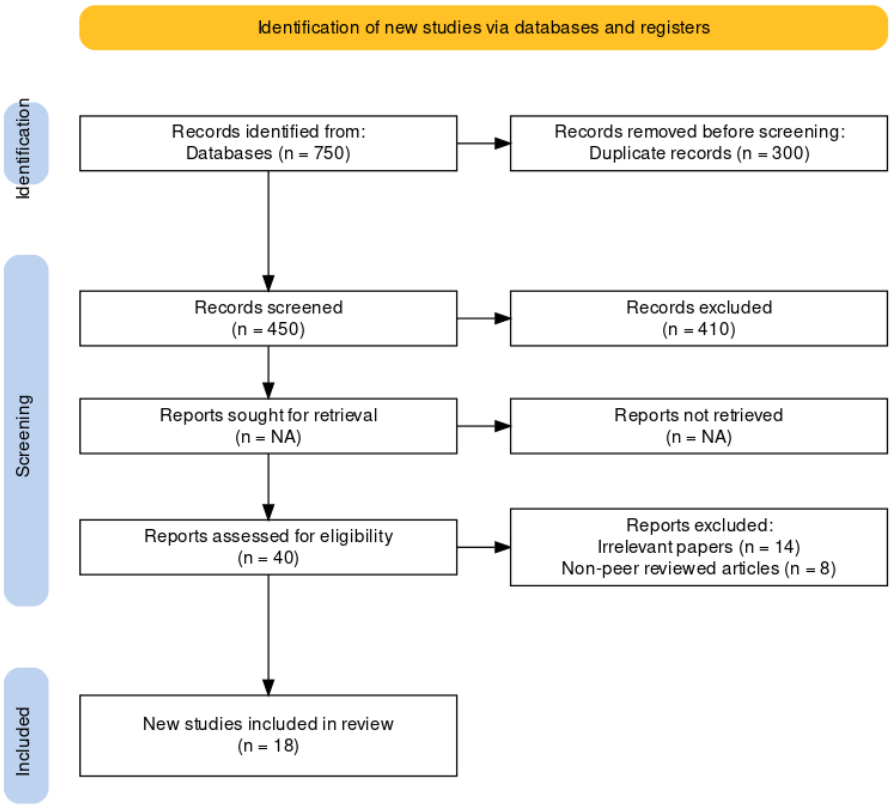

Figure 1. **The PRISMA flow chart of the literature selection for the systematic literature review (author's development)**

Discussion

Pakistan has a standard pharmaceutical distribution network. The pharmaceutical industry produces drugs, which are at that point moved to merchants and wholesalers, put away at retail areas or healthcare offices, suggested by doctors, managed at drug stores or restorative supply stores, and at last given to and expended by clients [19]. The Drugs Act of 1976 directs the purport of crude materials, fabricating, capacity, dissemination, and deal of drugs all through the country (XXXI of 1976). The Sedate Administrative Specialist of Pakistan (DRAP) is mindful for guaranteeing that the Drugs Act of 1976 is executed [19, 23]. The DRAP contains a committee on the accessibility of life-saving drugs that bargains with therapeutic deficiencies especially. Need of execution of existing approaches, a tireless arrangement crevice between the pharmaceutical industry and the wellbeing segment, a hurried enlistment prepare, a lack of cost control, a need of a web notice framework, and inadequately sentencing strategies for non-compliant partners are what cause pharmaceutical deficiencies in Pakistan, in spite of the nation having an administrative specialist [24, 25]. Within the private division, sound medicine is "famously troublesome," concurring to the World Wellbeing Organisation, since of variables counting quiet request, medicine advancement, and sedate vendors' self-interest in making a benefit. According to the research, interventions that are suited for improving practises may be sustained and become more affordable if they are scaled up [26]. The issue is widespread and ingrained. Due in part to a lack of understanding of the scope of the issue and the associated financial and health consequences, few nations presently monitor the improper use of drugs, and decision-makers frequently lack the knowledge necessary to address this issue in the most efficient manner. Whereas this can be going on, a few countries need the human and budgetary assets essential to energise more exact demonstrative procedures, to put in put viable control of medicine and apportioning behaviour, and to empower persistent adherence to treatment in both the open and private divisions. Additionally, the high cost of medications makes it difficult for patients to stick to suggested dosages; according to some research, 90% of consumers purchase antibiotics for three days or less [27].

According to another source, the minimum number of prescription medications documented was 5, exceeding the WHO guideline of two prescription drugs. This only demonstrates the tendency among doctors towards polypharmacy, which is a significant contributor to irrational usage. The dosage of a drug and its side effects are closely related. Up to 22% of dose mistakes, which account for 50% of reported side effects that might have been avoided, were the most frequent form of prescription errors. Additionally, this study reveals significant frequencies of medication interactions and duplication. Patients had to pay for 70% of the medications. The high cost may cause therapeutic non-adherence. It has been noted that prescribing many antibiotics–typically third generation

antibiotics—was a regular practise. The primary cause of the evolution of bacterial infections with resistant strains is the overuse of antibiotics [28]. A study publication reported that 31% of medications had incorrect dosage or did not specify how often they should be taken. Both are crucial for the most effective therapeutic approach. The length of treatment, which is significant for the administration of a few disarranges counting jungle fever and anti-microbial treatment, was not said when 12.56% of solutions were managed. It was discovered that the prescription contained superfluous medications with no indication. It was observed that the patients had a variety of illnesses, and the prescription's treatment of certain issues was completely disregarded [29].

According to WHO recommendations, each medication should have an appropriate label that includes the patient's name, the dosing schedule, and the medication itself. Even though it is very desirable that all pharmaceuticals be correctly labelled, a survey revealed that just 3.96% of them were. It was discovered during patient interviews that the majority of them were unsure of the precise timing of their medication intake. In three of the four facilities, not even one medicine had the necessary labelling. Unfortunately, compared to the desired value of 100%, the patient's awareness of the proper dosage of medications was low (54.98%) [30]. Agreeing to a journal, the normal rate of nonexclusive drugs endorsed was 29.7%, which is lower than the WHO benchmark values of 100% and outlines the doctors' inclination for brand-name medicines. While the WHO's International Networking for Rational Use of Drugs (INRUD) set a limit of up to 30%, the average proportion of administered antibiotics was 64%, demonstrating how all healthcare institutions contribute to bacterial resistance to antibiotics. In Punjab, patient counselling was not performed prior to dispensing during the average dispensing time of 88.5 seconds in hospitals. In Punjabi hospitals, 82.9% of prescriptions were really filled; hence the remaining patients were directed to local pharmacies for their medication needs. Due to low literacy and carelessness during the prescription and administration of medications, there were only a small proportion of patients who accurately knew the amount of their medications [31].

According to a self-administered, descriptive cross-sectional survey, the most prevalent conditions for which people use drugs without first consulting a doctor are headache (96.52%), fever (80%) and minor cuts and wounds (85%). The self-medication is more common with drugs used for minor injuries than it is with antibiotics. The survey participants saw the print and electronic media advertising as a source of encouragement for self-medication with OTC headache medications in addition to cough, cold, and fever. However, this study exposes a dangerous scenario in which some individuals misuse cough and cold medications to induce sleep in a compulsive manner, despite the fact that insomnia was not professionally diagnosed in them. Concerns about the toxicity of cough syrups used for self-medication are growing. The previous research demonstrates that Pakistan's inappropriate prescription and usage of antibiotics has contributed to the evolution of resistant forms of bacteria [32]. The average consultation and medication dispensing times are insufficient for giving patients advice on how to use their medications, and the safety and storage requirements for dispensing are insufficient. In the private sector particularly in rural regions, irrational usage is more pronounced. Evidence shows that 6–11% of people regularly use antibiotics for self-medication [33]. It is widely acknowledged that a rational drug usage is the crucial component of health policy. The guiding concepts or criteria are efficacy/effectiveness, accessibility, and safety. Irrational drug usage can take many various forms, such as when prescribed medications are unavailable or when a prescription is written incorrectly. The access to drugs is another issue while trying to maintain or enhance health. Additionally, it raised the mortality and morbidity rates and encouraged the use of sterile injections, which widened the range of blood-borne illnesses like hepatitis. Within the constraints of the available resources, we must enhance the responsible use of pharmaceuticals in order to reduce these issues. The WHO first proposed the "Essential drug" idea in 1970, arguing that a small number of pharmaceuticals would result in improved drug supply, better prescription, and cheaper healthcare costs [34].

There are genuine drug-related issues in Pakistan. Whereas the showcase is overwhelmed with strange pharmaceuticals, numerous of the "Fundamental Drugs" that frame the premise of sound endorsing are not promptly accessible. A record number of formulations—about 50,000—have been registered in Pakistan. The problem is made worse by the market's unfettered distribution of fake and outdated medications. Studies conducted by the editorial's author on prescription patterns revealed a very high rate of medication abuse and illogical usage by doctors in Pakistan's public and private sectors [35]. Common instances of irrational drug use include prescribing excessive amounts of medication (polypharmacy), injecting patients when oral medication is sufficient, prescribing antibiotics with inappropriate dosages and treatment durations, disregarding proper clinical guidelines when writing prescriptions, and patients who fail to follow treatment plans in full or self-medicate. The socioeconomic situation in a poor and growing nation like Pakistan is unsatisfactory, and individuals need to be informed on how to utilise medications properly as well as paramedical workers. The consequences of irrational drug use include inappropriate drug prescribing that may increase morbidity or mortality rates, lead to drug resistance, or waste resources and essential medications, increase the availability of or prescription for drugs with a disproportionately high number of side effects, and influence patient behaviour that there must be a drug for every ailment, which may result in irrational drug use [36, 37]. This systematic analysis indicates that regulatory processes for facility checks and Good

Manufacturing Practices (GMP) assessments, analytical labs, and capacity development all need to be improved in order to successfully control substandard and counterfeit medicine in Pakistan. The assertion that 40–50% of Pakistan's medications are of poor quality cannot be backed up by the information presently accessible. The main reasons community pharmacists offer subpar services are a lack of knowledgeable staff, a lack of advice, a lack of decorum on the part of the dispensers, as well as the ambiguity of the rules and how they are implemented.

Conclusions and Implications

In this review the situation of medicine in Pakistan has been examined.

1. The research suggests that in order to effectively regulate substandard and counterfeit medication in Pakistan, regulatory procedures for facility inspections and GMP assessments, analytical laboratories, and capacity building, all need to be strengthened.
2. The material that is currently available cannot support the claim that 40–50% of Pakistan's medications are of low quality.
3. The primary causes of the subpar services provided by community pharmacies include a lack of competent personnel, a lack of advice and a lack of professionalism on the part of the dispensers, as well as the vagueness of rules and how they are applied.
4. It is proposed that in arrange to assemble vital measurements around subpar and fake medications in Pakistan, efficient objective information must be created through well-planned, financed ponders.
5. The country is moving rapidly towards distant better administrative system, but for a smooth move to a well-regulated framework, it is necessary to have a complete, long-term vision that is interdisciplinary, open, dynamic, and evidence-based. Each exertion ought to be made by the government to energise the utilisation of basic medications in both the private and public sectors.
6. The government wellbeing offices and the government ought to do their hardest to kill that loathsome sickness and follow to WHO rules to ensure the proper medicine use in Pakistan.

Declarations

Author contributions

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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