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

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Abstract

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

Study design: Literature review

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

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

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

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

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

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Introduction

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

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

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

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

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

For those suffering from CKD, according to the Global Burden of Disease Study, there were as many as 5.5% of the general population with CKD in 2016. This corresponds to a 44% rise in CKD cases between 1990 and 2016, which included 1600 deaths, or about 1% of all 2016 fatalities [6]. Regarding management, another study

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

Research Problem

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

Research Focus

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

Research Aim and Research Questions

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

Research Methodology

General Background

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

Data Analysis

Information sources:

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

Data items:

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

Search strategy:

The search strategy is displayed in Table 1

Table 1. Search strategy on Pubmed

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

Research Results

Salient findings

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

Synthesis of studies

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

Table 2. Synthesis of studies

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

Understanding AKI in newborns globally

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

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

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

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

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

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

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

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

Discussion

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

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

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

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

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

Conclusions and Implications

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

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

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

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

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

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

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

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

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

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

Prospects for further research

Since this is a foremost study that attempts to assess the current status of acute renal failure management of new-borns in Kazakhstan, this article can serve as a pioneer and an example for others to dive into investigating the current state of affairs within the health sector of Kazakhstan, particularly with regards to the pediatric population, which are the most vulnerable. Prospective research can expand and cover management of other diseases that afflict new-borns and seek out any innovation by the Kazakhstan health sector that can be emulated by other countries.

Limitations

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

Declaration

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