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Risk Factors Associated with Acute Renal Failure in Neonates of a neonatal Intensive Care Unit

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Authors' contributions

This work was carried out in collaboration among all authors. Author AJUB started the idea for this project in his neonatology specialty and wrote the initial manuscript, collected information from the literature. Author AIVDLC did the Protol supervised and work in hospital. Author CTSP did the Supervision of work and Information collected from the literature. Authors SML and SHH did the Supervision of the manuscript and information of the literatura and supervised the references. Author JCRL did the analysis of the protocol, results and supervisión the writing of the final manuscript, revised the manuscript, structured the article. All authors read and approved the final manuscript.

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ABSTRACT

Objetive: Determining the risk factors associated with acute renal failure in neonates.
Materials and Methods: A case-control study was carried out, in 65 cases of acute renal failure and 65 without acute renal failure in the Intensive Care Unit Neonatals (NICU) of a hospital in Pachuca Hidalgo, Mexico. The variables studied; prematurity, low weight, type I respiratory distress syndrome, perinatal asphyxia, sepsis, necrotizing enterocolitis, administration of vancomycin, amikacin, amphotericin, cefotaxime and water restriction. The information was collected from the data of the clinical records and the analysis was carried out in the Epi-info software. The statistical analysis, it was performed using non-parametric tests such as Chi2 and Fisher's Exact Test.
Results: Denote underweight with an OR 2, 95% CI. from 1.1 to 3.3 and <P 0.05 by Chi2 and Fisher's exact test. For; perinatal asphyxia with OR 2.1, 95% CI. from 1.3 to 3.4 and <P 0.05 through Chi2 and Fisher's exact test. For vancomycin administration OR 4.7, 95% CI. From 2.3 to 9.3 and <P 0.05 by Chi2 and Fisher's exact test. For water restriction OR 2, 95% CI. From 1.2 to 3.3 and <P 0.05 by Chi2 and Fisher's exact test.
Conclusion: A significant association was found between acute renal failure with low weight, perinatal asphyxia, administration of vancomycin and water restriction.

Keywords: Acute renal failure; perinatal asphyxia; vancomycin administration; water restriction.

1. INTRODUCTION

Acute renal failure in neonatology is common, especially in preterm patients of low weight. The incidence is estimated in premature infants of 12.5%, up to 39.8% during the first weeks of life [1]. Nephrogenesis ends between 34 to 36 weeks of gestation, where 700,000 to 1,000,000 nephrons are reported in each kidney 2.

The kidney has three specific functions: regulate water and electrolyte balance, eliminate toxins, secrete hormones; if there is an injury, the homeostasis will be lost 2.

Urine production occurs from 10 to 12 weeks of gestation (SDG), the kidney manages to produce 10ml / kg / h of urine in the fetal stage. The glomerular filtration rate (GFR) is decreased at birth, but at 12 months of age, it is closer to that established in adulthood. Renal function can be measured by determining serum creatinine, however, in the first 72 hours maternal creatinine is reflected. The biochemical markers that can help us determine renal function with better accuracy is the glomerular filtration rate, and the clearance of creatinine and cystine, the latter is poorly accessible, due to increased cost and obtaining [2].

Renal function in neonatology can be measured specifically with the classification of acute renal injury in infants AKIN (Acute Kidney Injury Network), where serum creatinine and uresis is considered, which is what is being used in recent studies, and is determined as follows:

State l. Creatinine> 0.3mgdl or more than 150-200% increase in baseline, with uresis less than 0.5ml / kg / h for 6 hours.

State ll. Increase in creatinine greater than 200 - 300% of baseline with uresis less than 0.5ml / kg / h for more than 12 hours.

State lll. Increase in creatinine greater than 300% baseline or greater than 4mg / dl with an acute risk less than 0.5m / gdl and uresis for 12 hours. The following parameters are considered to classify the origin: urinary sodium, renal function index, and excreted sodium fraction (FeNa), it is considered intrinsic fault with FeNa value of 2.5-3; Prerenal failure in those older than 32 SDG <2.5, in infants aged 29-32 intrinsic renal failure> = 6 and prerenal <6. It is estimated that the percentage of prerenal renal failure is 85%; intrinsic or renal 10% [3].

Urinary sodium greater than 50 mEq / L suggests intrinsic FRA and less than 20 mEq / L suggests

prerenal FRA. During the decrease in glomerular filtration leading to oliguria, to maintain intravascular volume, sodium is reabsorbed at the tubular level, carrying water.

The renal function index (IFR) greater than 4 in term infants and greater than 8, in premature infants under 32 SDG suggests intrinsic ARF. Protein intake should be adjusted to the minimum requirements to meet the needs of basal growth (1-2 g / kg / day), keeping the BUN below the threshold and to cause increase in serum osmolarity [4].

Calorie administration may require the placement of a protein restriction central line with a high concentration of dextrose and lipids [5].

For hypotension use aminergic support such as dopamine, dobutamine; if it is for sepsis start norepinephrine, and for refractory shock due to sepsis add hydrocortisone [6].

The indices are obtained as follows:

* Renal function index = (Urinary Na x serum creatinine X 100) / Urinary creatinine.
** Excreted sodium fraction = (Urinary Na x serum creatinine X 100) / (Serum sodium x urinary creatinine) [7].

There must be a strict control of liquids, for this it is necessary to monitor the weight, quantify uresis with urinary catheter not less than 0.3ml / kg / h for more than 24 hrs. or anuria, monitor serum electrolyte levels[8].

Dopamine at lower doses has been shown to improve renal perfusion by stimulating the D1, D2 and D4 receptors, [7] although it has not been proven that it has a substantial impact on the outcome in adult and pediatric populations, but it has been shown to temporarily improve urinary production and serum creatinine in neonates [8].

Currently, evidence suggests that loop diuretics should not be used to prevent ARF, although in cases of fluid overload with oliguria / anuria they do provide a reasonable therapeutic option [9].

Renal replacement has not been shown to be useful in the long term because of the comorbidity and mortality involved [10,11].

The overall incidence of ARF among NICU patients ranges from 8% to 24% (1-7) [12,13].

The incidence of acute renal failure in premature infants is 12.5% to 39.8% during the first weeks of life [1,14].

A study by Viswanathan et al. Reported that in the term infants, the main causes of acute renal failure (ARF) are congenital anomalies of the kidneys and urinary tract (CAKUT), post-surgical complications, hypothermia, obstructive uropathies and systemic disorders (birth asphyxia) / metabolic. While in the preterm population, poor renal perfusion due to hypotension, sepsis, necrotizing enterocolitis (NEC), persistent ductus arteriosus and nephrotoxic medications play an important role [1].

In a study conducted by Montaz et al, which was cross-sectional, the risk factors associated with acute renal failure were determined, considering the diagnosis for hospitalized newborns, if the serum creatinine level was> 1.5 mg/dl. In total, 49 of 3166 infants (1.54%) were diagnosed as ARF who entered the study consecutively. Of 49 newborns with ARF, 43 (87.8%) were female and 6 (12.2%) were male. The average age of the patients was 7.4 ± 6.2 days and the average weight of the babies with ARF was 3510 ± 680 g. 39 patients (79.5%) were term infants. The most common causes of ARF, in order of prevalence, included sepsis (77.5%), followed by hypovolemia secondary to dehydration (46.9%), hypoxia secondary to respiratory distress syndrome (RDS) (34.6%), persistent arterial duct (CAP) (8.1%), posterior urethral valves (PUV) (6.1%), asphyxiation (4%) and renal venous thrombosis (RVT) (2%). Sepsis and the incidence of ARF were significantly related (P=0.03). A mortality of 36.7% was reported [15].

Renal failure occurs in 50-12% of infants with asphyxiation, usually transient that recovers at 7 days [16,17]. Some of the effects of suffocation were analyzed in a study where it was observed that hypoxia and endotoxin are accompanied by histological changes in renal tissue and there is a significant decrease in the proliferation marker [18]. Within the mechanisms involved, ischemia reperfusion injury (IRI) is the predominant cause of acute renal injury [19].

Asphyxia and renal failure have been observed an incidence of 50% and 72% [20]. In a study by Karlo et al, in India they determined the association of neonatal asphyxiation and acute renal function, described asphyxiation with umbilical cord gasometry criteria with ph <7,

Apgar 6 to 5 minutes, liquid stained with meconium, variations in fetal heart rate, clinical evidence of hypoxic-ischemic encephalopathy; Renal function was determined using urine and blood sample 72 hours after birth. An asphyxiated neonate was considered to have acute renal injury if three or more of the following criteria were observed: urine production <0.5 ml / kg / h, blood urea> 40 mg / dl, serum creatinine> 1 mg / dl, presence of significant hematuria or proteinuria. FRA was considered prerenal if FENa <3 and intrinsic if FENa> 3. Infants with severe asphyxiation are more likely to experience renal failure than those with milder asphyxiation. Renal failure occurred in 14 of the 36 (39%) moderately asphyxiated infants and in 14 (100%) infants with severe asphyxiation [21]. Another study was conducted by Kaur S et al; where they evaluated glomerular function using the AKIN system classification for ARF and tubular function in newborns with moderate to severe asphyxiation. We included All neonat > 34 weeks' gestation with Apgar minute scores were reported. Birth asphyxia was defined according to the National Neonatology Forum of India, that is, an Apgar score of 7 to 1minute, moderate birth asphyxiation with an Apgar score between 4 and 6 to 1 minute and severe asphyxiation at birth, 3 1minute A total of 2196 neonates were born during the study period. We studied 36 infants who met inclusion criteria, presented moderate birth asphyxia in 11 (30.6%) and severe asphyxiation at birth in 25 (69.4%). FRA developed in one of 11 infants (9.1%) with moderate asphyxiation and in 12 of 25 (56%) with severe asphyxiation, with a total incidence of 41.7%. The FRA persisted in 16.6% of infants at 96 hours of life. Ten children (27.7%) had serum creatinine levels> 1.5 mg / dl. Those whose creatinine was 1.5 mg / dl within 6 hours of life took longer to reach a level than those in which it rose after 6 hours of life. The AKIN classification is useful for assessing acute renal failure in neonates with birth asphyxiation [22]. Severe sepsis such as the septic picture associated with organic dysfunction, arterial hypotension (is systolic blood pressure of less than 90 mmHg or a decrease of more than 40 mmHg from baseline, in the absence of other causes of hypotension) and hypoperfusion, septic shock [23,24].

In a study conducted by Montaz, he reported that sepsis was the most common predisposing factor for LRA in 77.5% of patients (n=38) accompanied by the highest mortality rate among other factors (30.5%) [25,26]. Sepsis is defined as the systemic inflammatory response to infection.

Understanding systemic inflammatory response data are the following:

Tachypnea, whining, retraction, desaturation / Thermal instability <36 ° C,> 37.9 °, HR> 2DE for age / Leukocytes <5000 or> 34000 / Bands> 10% [27].

A study by Sreekanth Viswanathan and Bindu Manyam, which included 59 infants who developed acute renal failure, out of a total of 472, in the period from 2000 to 2008, the average age was 24.7 SDG + -1.8, and weight 614 + - 128 grs, found that high pressures in ventilation, arterial hypotension, and use of cefotaxime, in neonates with extremely low weight increased mortality [1].

In a study conducted by Weintraub et al, they determined the risk factors for acute kidney injury in premature infants based on the time of onset, it was retrospective, the characteristics of newborns with and without FRA were compared using chi- square tests and t. renal failure occurred in 30.3% of 357 newborns; 72.2% were stage 1. Gestational ages, initial Cr, maternal magnesium and volumetric resuscitation were associated with early renal failure <1 day. Volumetric resuscitation, umbilical arterial line and the reception of a non-steroidal anti-inflammatory drug were associated with an intermediate renal lesion (days 2 to 5). And necrotizing enterocolitis and sepsis were associated with late FRA greater than 6 days [28,29].

Arcinue et al conducted a retrospective study of the clinical history of all infants with acute renal injury, according to the AKIN criteria, admitted to the NICU between 1998 and 2008. Case controls were matched for low weight, gestational age and date of birth, the associated risk factor was the presence of maternal placental abruption / hemorrhage, grade III or IV [30]. In a multicenter study conducted by Jetton et al, it was reported that a gestational age of 22 weeks to less than 29 weeks showed proportionately more acute renal failure events after the first week than those of the two older age groups [31]. The use of nephrotoxic drugs in the neonatal intensive care unit is very common; However, the effects of drug nephrotoxicity on short and long-term outcomes remain poorly studied, and it is

important as it would prevent preventable comorbidities [32].

A study was conducted where they analyzed the incidence of acute renal failure and vancomycin, the overall incidence of ARF was 2.7%, a comparison was made using the Mantel-Haenszel Chi-Square test showed a statistically significant association between the increase in minimum concentration of vancomycin and the incidence of ARF [33].

Aminoglycosides have been considered potentially nephrotoxic, but depending on the dose, and the time of administration, a study was conducted where it was observed that the incidence of high minimum levels of S-gentamicin increased among very premature newborns. No evidence of ototoxicity or nephrotoxicity was observed. This simple regimen of 5 mg / kg gentamicin during the first three days should be considered for all infants, as it potentially minimizes the risk of dosing errors and bacterial infection [34]. Amikacin is a nephrotoxic drug, which is frequently used in neonatal intensive care units, a study was conducted that showed improvement in nephrotoxicity related to decreased oxidative stress with the administration of vitamin E and erythropoietin, as antioxidants, which could be renoprotective [35].

Amphotericin is considered nephrotoxic, a study was conducted where it was observed that neonates with normal basal renal function appeared to tolerate lipid amphotericin B, relatively well. A sodium intake of 4 mEq / kg / day can significantly reduce the nephrotoxicity of this medicine [36]. Within some of the mechanisms of acute renal failure in neonates, it is because they are more likely to develop vasomotor nephropathy, at an early age the causes include hypotension, hypovolemia, perinatal asphyxiation hypoxemia, and neonatal septicemia[37].

Vachvanichsanong, reported in a study within the main etiologies of acute renal failure in newborns under 2 days were hypovolemia, in addition to sepsis and asphyxiation at birth [38,39], is related to what was reported by Youssef D et al, where 29.6% of the cases of ARF were obtained had oliguria and the male sex prevailed, with a proportion of men and women of 1.3: 1, where the cause of the ARF was pre-renal in 96.3% [40]. In a recent study that was carried out, it is said that the pre-renal form is the most common, with variable contributing factors of which mechanical ventilation and sepsis were the most common, however, it was not possible to perform specific association [41].

The incidence of acute renal failure is very high, reaching reports of 24%, with a high mortality rate, due to the metabolic alterations that it entails, such as hyperkalemia, as well as anasarca, cardiopulmonary congestion, in our country there has been little studied in neonates, so it is important to recognize the risk factors associated with acute renal failure in neonates of our intensive care units, in order to take timely action, and intentional search for renal injury, giving the infant a lower morbidity and mortality, improving the forecast in the short and long term.

Objetive: To determine the risk factors associated with acute renal failure in neonatal intensive care neonates of Pachuca General Hospital.

H_A Hypothesis: The association of prematurity, low weight, perinatal asphyxiation, water restriction during the first 7 days of life, neonatal sepsis, necrotizing enterocolitis, type 1 respiratory distress syndrome, antimicrobial administration, will be statistically significant in patients who present with acute renal failure.

H_0 Hypothesis: The association of prematurity, low weight, perinatal asphyxiation, water restriction during the first 7 days of life, neonatal sepsis, necrotizing enterocolitis, type 1 respiratory distress syndrome, administration of antimicrobials, will not be statistically significant in patients presenting with acute renal failure.

2. MATERIALS AND METHODS

A case-control study was carried out in 65 cases and 65 newborn controls, the cases were patients with acute renal failure, and the controls patients without renal failure, the associated risk factors were determined. The data were compared using the Epi-info statistical software, using non-parametric statistical methods for nominal variable $\chi 2$ for 2 samples, and non-parametric association, for nominal variables and for descriptive inferential OR, based on the results it was considered statistically significant with OR greater than 1. It will be considered significant association with significant $p<0.05$. in patients of the general hospital of Pachuca during the months March-September 2018.

2.1 Selection of the Study Population

Case Inclusion Criteria	Case Exclusion Criteria	Removal criteria the cases	Inclusion criteria of the control group	Control exclusion criteria	Control Elimination Criteria
-Newborns at the General Hospital of Pachuca and admitted to the NICU. -Infants weighing more than 500grs. -Infants with acute renal failure (Creatinine> 0.3mg / dl or more than 150-200% increase from baseline, with uresis less than 0.5ml / kg / h for 6 hours or more).	-Infants who confirmed renal failure due to congenital renal malformation.	-Neonates with incomplete records.	-Newborns in the General Hospital of Pachuca and admitted to ucin. -Infants weighing more than 500grs. Infants who did not have acute -renal failure.	-Infants who confirmed renal congenital malformation.	Infants who died before discharge or complete neonatal period (28 days).

2.2 Sample Size

The Epi-info software was calculated, considering the annual population of newborns admitted to NICU in an average of 350 patients according to what was recorded in the income and discharge control book, of these, the estimated prevalence of renal failure according to the literature is 24% (n84). The sample size was calculated with a 95% confidence level, with a 5% confidence limit. Total sample size of 65 cases. 1 control was taken per 1 case. Non-probabilistic sampling, for convenience, by including consecutive cases and 1 control for each case.

3. RESULTS

After 7 months of conducting the study where a total of 130 newborns were obtained, of which 65 belonged to the case group and 65 to the control group. In 45% (n = 5) of the newborns were women and 55% (n = 71) were men.

The average gestational age was 33.8 SDG (weeks of gestation), 70% (n = 91) were premature and 30% (n = 39) terminated. Regarding the presence of renal insufficiency, 42% of premature patients had renal failure. Regarding the distribution of premature infants and children in terms of cases and controls, there were premature infants with renal failure 42% (n = 54%), premature infants without renal failure 28% (n = 37), term infants with renal failure 8% (n = 11), term infants without renal failure 22% (n = 28) (Fig. 1).

Regarding associated risk factors, the relative risk was determined. Among the risk factors, patients with amphotericin and patients with necrotizing enterocolitis had initially been considered, however, only 1 of the patients used amphotericin and 8 presented with necrozant enterocolitis, so the sample was not significant, so decided to eliminate these 2 variables (Table 1).

It was obtained as a significant risk factor low weight with an OR 2, lower 1.1; perinatal asphyxia with OR 2.1, lower 1.3; Vancomycin OR 4.7, lower 2.3; water restriction 2, lower 1.2; and relative risk sepsis with OR 1.05, SDR type I with OR 1.1, Cefotaxime 1.1. Table 2.

Non-parametric tests were performed, the results are shown in (Table 3).

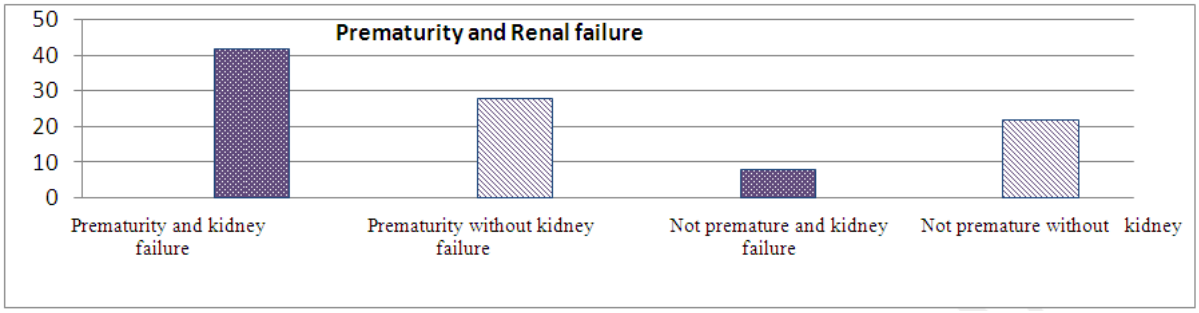

Fig. 1. Presence of renal failure in neonates with prematurity, March-September 2018 period, in the neonatal intensive care unit of the General Hospital of Pachuca.

Note: The neonates who presented prematurity and renal failure are represented, and those who did not present it

Table 1. Report patients with and without renal failure

	Cases		Controls	
Variable	Si	No	Si	No
Prematurity	54	11	37	28
Low weight	21	44	23	42
Perinatal asphyxia	25	40	11	54
Sepsis	34	31	29	36
ECN	1	64	7	58
Type 1 SDR	41	24	16	49
Amikacin	64	1	52	13
Vancomycin	10	55	18	47
Amphotericin	0	65	1	64
Cefotaxime	31	34	28	37
Water restriction	27	38	11	54

Note: NEC (Necrotizing Enterocolitis); SDR type I (respiratory distress syndrome type I).

Table 2. Analysis of raw OR and 95% CI of NC of the variables studied.

Variable	OR	95% CI	95% CI	Chi2
	OR	Inferior	Superior	p
Prematurity	0.51	0.32	0.81	0.004
Low weight*	2	1.1	3.3	0.011
Perinatal asphyxia*	2.1	1.34	3.44	0.0016
Sepsis	1.05	0.64	1.74	0.904
Type 1 SDR	1.19	0.78	1.8	0.4606
Amikacin	0.2031	0.1026	0.3725	<0.05
Vancomycin *	4.7	2.375	9.3	<0.05
Cefotaxime	1.1935	0.7205	1.9894	0.5443
Water Restriction *	2	1.238	3.3023	0.0039

*Note: * Variables associated with acute renal failure. A risk factor associated with acute renal failure, an OR> 1, 95%CI including the unit and the value of p <0.05 was considered by non-prametric tests such as Chi 2 and Fisher's Exact Test.*

It is observed with p <0.05, the variables such as prematurity, low weight, perinatal asphyxia, amikacin, vancomycin, water restriction. However, the variables low weight, perinatal asphyxia, vancomycin, water restriction was those that met the following 3 criteria: OR greater 1, 95% CI, and p less than 0.05.

4. DISCUSSION

Acute renal failure is an important cause of comorbidity in the neonatal intensive care unit, reporting up to an incidence of 39.8% in the first weeks [4]. The objective of the study was to determine the risk factors associated with acute renal failure in neonates, an average gestational

Table 3. Non-parametric tests in risk factors associated with acute renal failure in neonates

Variable	X2	p	Fisher
Prematurity *	7.6	0.004	0.0027
Low weight *	6.34	0.011	0.005
Perinatal asphyxia *	9.92	0.0016	0.00073
Sepsis	0.014	0.904	0.45248
Type 1 SDR	0.544	0.4606	0.23039
Amikacin *	32.4675	<0.05	0
Vancomycin *	22.7368	<0.05	0.00000038
Cefotaxime	0.3676	0.5443	0.2723
Water Restriction *	8.3457	0.0039	0.001798

Source: Data collection sheets

age was observed in patients with acute renal failure of 32.3 SDG, with an average weight of 1596 grs, compared with a study conducted by Montaz et al. [19], who reports the majority of infants with renal failure, to term infants, and with an average weight of 3510 grams, a significant difference in the population is observed, in our study, the majority of patients with renal failure, was Preterm and low weight. In contrast to a study by Viswanathan et al [1], which included 59 infants who developed acute renal failure, where the average age was 24.7 SDG, and the weight 614 grams. Regarding the sex of the patients, the majority were 87.8% women, in our study a higher incidence was reported in 55.4% in men. Prematurity was not associated with renal failure, but low weight for gestational age did present an association with acute renal failure. Within the risk factors described by Montaz et al. [19], sepsis and the incidence of ARF were significantly related [41], in our study sepsis was relatively associated, but was not significant. In a study by Karlo et al [25], in India they determined the association of neonatal asphyxia and acute renal function, as well as Kaur S et al [25], reported an incidence of acute renal failure in a total of 41.7% in patients with perinatal asphyxia; corroborating this association in our study, with a relative risk of 2.1 times the possibility of presenting acute renal failure, if perinatal asphyxia occurs, with a p <0.05.

The type 1 respiratory distress syndrome due to surfactant deficiency showed a relative association, however this was not significant. Among nephrotoxic drugs, it was significantly associated with vancomycin administration with a relative risk of 4.7, and p <0.05, according to the association described by Bhargava et al [28] in their study. Cefotaxime only presented a relative risk of 1.1, being non-significant, with p> 0.05, the administration of amikacin, in our study it is not related to a higher risk of acute renal failure in neonates. Regarding the water restriction, the association was significant with a relative risk of 2 times greater, p <0.05, this could be due to hypovolemia, and secondary acute renal failure, which should be considered, the recommended strict water supply, of according to each gestational age, and specific patient, considering water balance, to reduce this risk factor in neonatal intensive care units, we agree in this variable with the study reported by Vachvanichsanong et al [41], where hypovolemia was reported as a risk factor of acute renal failure in the first days of life.

The association was comparative in the variables, low weight, perinatal asphyxia and water restriction, of these the water restriction is something that can be adequately managed in the neonatal units and decrease the incidence of acute renal failure. Acute renal failure in the neonatal intensive care unit (NICU) apparently in Mexico has not been adequately studied. It is possible to transcend in this study since if it is detected early, the cause can be analyzed, often reversible and avoid chronic renal failure, even death, since a high mortality rate of this disease is reported (20-50%).

It is important to detect this pathology in the early stages to determine actions that allow us to provide adequate and timely treatment, so that we can act early and prevent renal failure from passing to the terminal phase, since the management of end-stage renal failure in neonates is not very encouraging. Due to the deficiencies that currently exist and the little evidence of improving the morbidity and mortality of renal function replacement therapy such as peritoneal dialysis or hemodialysis, the high economic cost, impacting the family and public economy.

Therefore, the results of this research allow establishing the risk factors associated with

acute renal failure, which impacts considering being able to take actions that help to reduce the incidence and therefore morbidity and mortality in the neonatal intensive care unit of the Pachuca General Hospital, thus impacting the future of patients and their families.

5. CONCLUSIONS

-An association between renal failure and perinatal asphyxia was detected, in the same way with low weight and with the administration of vancomycin, and there was even a significant association between acute renal failure and water restriction during the first 7 days of life.
-No association is detected between acute renal failure and neonatal sepsis, as well as prematurity and respiratory distress syndrome.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICAL APPROVAL AND CONSENT

The study was carried out according to, Helsinki Declaration of the World Medical Association were respected, the General Health Law, the local rules, and regulations of the country, as research work for the academic program of medical residences. According to article 17, the study that was carried out is considered without risk, since it is not involved in procedures or patient management, it was only documentary investigation on file, and it was dispensed to obtain informed consent according to article 23.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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