Decreasing incidence of renal cortical necrosis in patients with acute renal failure in developing countries: a single-centre experience of 22 years from Eastern India

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Abstract

Background. Renal cortical necrosis (RCN) accounts for 2% of all cases of acute renal failure (ARF) in adults and 15–20% of ARF during the third trimester of pregnancy in developed nations. However, RCN incidence is higher in developing countries ranging from 6–7% of all cases of acute renal failure. The present study describes changing trends in the clinical spectrum of RCN in patients with ARF in Eastern India.

Methods. Patients with ARF suspected to have RCN on clinical grounds underwent percutaneous renal biopsy. Patients showing cortical necrosis on histology were included in the present study. Diffuse and patchy cortical necrosis was classified based on standard histological criteria. The patients with cortical necrosis were studied over a period of 22 years; from July 1984 to December 2005. The results of our observation were compared with respect to etiology, incidence, prognosis and outcome of renal cortical necrosis in two study periods; namely, 1984–1994 and 1995–2005.

Results. The incidence of RCN was 3.12% of all cases of ARF of diverse etiology. RCN was observed in 57 patients; obstetric 32 (56.2%); non-obstetric 25 (43.8%). Diffuse cortical necrosis was the dominant lesion in 41 (71.9%) patients and the remaining 16 (28%) patients had patchy cortical necrosis. The overall incidence of RCN in obstetric ARF was 15.2%; the incidence being higher (11.9%) in the post-abortion group in comparison to 3.3% in late pregnancy. RCN had occurred complicating abruptio placentae, puerperal sepsis and postpartum haemorrhage (PPH) in late pregnancy, while septic abortion was the sole cause of RCN in early pregnancy. Haemolytic uraemic syndrome (HUS) was the major (31.5%) cause of RCN in the non-obstetric group and miscellaneous factors were responsible in seven (12.3%) patients. Partial recovery of renal function was observed in 11 (19.2%), and 16 (28%) patients had progressed to ESRD. The incidence of RCN decreased from 6.7% in 1984–1994 to 1.6% in 1995–2005 of total ARF cases. RCN following obstetrical complication decreased significantly; 4.7% in the 1990s to 0.5% of the total ARF cases, in the 2000s. The mortality decreased to 19% in 1995–2005 from the initial high mortality of 72% in 1984–1994. The renal prognosis improved as a result of the decreased mortality of patients.

Conclusion. We observed a decreasing trend in the incidence of RCN in patients with ARF in recent years, which is associated with increased patient survival and better renal prognosis. This improvement was mainly due to declining incidence and severity of RCN in obstetrical ARF.

Keywords: acute renal failure; developing countries; haemolytic uremic syndrome; pregnancy; renal biopsy; renal cortical necrosis

Introduction

Renal cortical necrosis (RCN) is a rare cause of acute renal failure (ARF) in developed countries, but still occurs in developing countries due to poor health facilities. RCN is usually extensive, although focal and localized forms occur. RCN occurs in two peaks, the first peak in early infancy due to severe perinatal events or condition and the second peak occurs in women of childbearing age due to obstetric causes. The frequency of RCN in all patients with ARF is 1.9–2% [1–3] in western countries, in contrast to more than 7% of
patients with ARF in developing countries [4–6]. In an autopsy series, incidence of RCN was found to be 0.2% in a study of 11 800 autopsies [7]. RCN was observed by postmortem examination in 0.5% of infants aged 3 months or younger at death [8]. With improvement in health care systems in developing countries the incidence of RCN is expected to decrease. The purpose of this study was to review the clinical spectrum of RCN at our centre from July 1984 to December 2005 and to compare our results in two study periods; 1984–1994 and 1995–2005. We also highlight decreasing trends in the incidence of RCN in later periods.

Material and methods

This study was carried out in the Department of Nephrology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India over a period of 22 years; from July 1984 to December 2005. The study was divided into two 11-year periods; 1984–1994 and 1995–2005. The results of our observation were compared with respect to etiology, incidence, renal prognosis and outcome of patients with RCN in these two periods. The demographic data, clinical presentation, laboratory investigations, underlying etiology, need of dialysis, course of disease and outcome were recorded in individual patients. Based on urine volume absolute anuria was defined as no urine output or only a few drops of urine in 24 h. Anuria was considered when urine output was less than 100 ml in 24 h. Renal biopsy was performed in patients with ARF who had persisting oligoanuria or severe degree of renal failure or prolonged renal failure (>4 weeks) to confirm the diagnosis of RCN. The ARF patients with biopsy-proven RCN were included in the present study. RCN was divided into two groups using standard histological criteria:

(i) Complete cortical necrosis: Confluent global cortical destruction extending into the columns of Bertin. The thin rim of subcapsular and juxta-medullary tissue may be preserved. Irreversibility of renal function is the rule in complete cortical necrosis.

(ii) Patchy cortical necrosis: Contiguous area of cortical necrosis involving one-third to half of the entire cortical tissue. This form has potential for partial recovery of renal function.

Data were compiled over a period of 22 years and were further analysed broken down into two 11-year periods, i.e. 1984–1994 and 1995–2005 to find the changing pattern in incidence, etiology and outcome of RCN in patients with ARF.

Statistical analysis

The statistical significance of difference between two study periods (1984–1994 vs 1995–2005) was evaluated using the ‘Z’ test and chi-square test. The P-value of <0.05 level was selected as the point of statistical significance.

Results

Of 1822 patients with ARF, 57 (3.12%) cases had RCN. The age of patients in the obstetrical group ranged between 20 and 38 years. The age range of patients in the non-obstetric group was 18–55 years. The age of children with HUS was 8 months to 12 years. The vast majority of patients with RCN were female, 43 (75.4%) and 14 (24.6%) cases were male. RCN due to obstetric causes was seen in 35 (56.2%) and non-obstetric causes in 25 (43.8%) patients. Diffuse and patchy cortical necrosis were seen in 41 (71.9%) and 16 (28%) patients, respectively (Table 1).

All patients with RCN had severe renal failure at presentation. Oligoanuria of 5–12 days duration was seen in all (absolute anuria 45; anuria 12) patients. The other presenting features included the following: neuropsychiatric complications (22), metabolic acidosis (15), fluid overload (9), bleeding diathesis (5), hyperkalaemia (3) and pericarditis in one patient. Of 210 obstetric ARF, RCN was observed in 32 (15.2%) cases. RCN due to obstetric causes predominantly occurred following septic abortion in 25 (78%) patients. Haemolytic uraemic syndrome (HUS) was the main cause of RCN (72%) in the non-obstetric group. It is evident that obstetric complications and HUS were the major causes of RCN in patients with ARF. Of 18 cases of HUS, 12 (66.6%) patients had HUS in association with diarrhoea (D + HUS) and the remaining six (33.3%) patients did not have diarrhoea prodrome (D-HUS). The HUS not related to diarrhoea prodrome (D-HUS) was seen in adult patients only. Septic abortion and HUS contributes to 1.7% and 0.98% of RCN, respectively, of total cases of ARF (Figure 1). The mean peak BUN and serum creatinine were 80 mg/dl and 12 mg/dl respectively. Dialysis support was needed in all patients (peritoneal/haemodialysis) along with supportive treatment.

Comparing the data in two 11-year periods (i.e. 1984–1994 and 1995–2005), the incidence of RCN in 1984–1994 was 6.7% of all ARF cases and it decreased to 1.6% in the 1995–2005 period. The mortality decreased from 72% in 1984–1994 to 19% in 1995–2005. Total number of ARF cases admitted in the first 11-year period was 536. Obstetric ARF was seen in 76 (14%) cases. RCN was observed in

<table>
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<th>Table 1. Demographic data</th>
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<tr>
<td>Duration of study (years)</td>
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<tr>
<td>Total ARF patients</td>
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<tr>
<td>Total number of RCN patients</td>
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<tr>
<td>Male: Female</td>
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<tr>
<td>Obstetric RCN</td>
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<tr>
<td>Non-obstetric RCN</td>
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<tr>
<td>Obstetric ARF</td>
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<tr>
<td>RCN of obstetric origin</td>
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<tr>
<td>RCN in early pregnancy</td>
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<tr>
<td>Type of cortical necrosis</td>
</tr>
<tr>
<td>Diffuse cortical necrosis</td>
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<tr>
<td>Patchy cortical necrosis</td>
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36 (6.7%) patients and mortality was 72%. Total number of ARF cases was 1286 in 1995–2005. Obstetric ARF was noted in 134 (10.4%) patients. RCN was observed in 21 (1.6%) patients and mortality was 19%. Thus, RCN decreased to 1.6% in 1995–2005 from 6.7% in 1984–1994. We also observed a significant decrease in mortality from 72% in 1984–1994 to 19% in 1995–2005 (Figure 2). Eleven (19%) patients showed partial recovery of renal functions and were off dialysis, and 16 (28%) patients progressed to ESRD. The observed difference in two study periods, 1984–1994 vs 1995–2005, in relation to incidence of obstetric ARF, RCN, mortality and outcome of patients with RCN was statistically significant (Table 2).

Discussion

RCN is a rare cause of ARF secondary to ischaemic necrosis of the renal cortex. The lesions are usually caused by significantly diminished renal arterial perfusion secondary to vascular spasm, microvascular injury, or intravascular coagulation. RCN is usually extensive and bilateral, although focal and localized forms may occur. RCN is a rare entity in developed countries, accounting for less than 2% of all cases of ARF [1–3]. RCN incidence is higher in developing countries, ranging 6–7% of all cases of ARF [4–6]. We have reported RCN in 23 (6.3%) patients with ARF in our previous study [4]. The incidence of RCN was 7.1% in patients dialyzed for ARF in the Chandigarh study [6,9]. The declining trends (3.8–4.6%) in incidence of RCN in Indian patients with ARF were reported in two studies [10,11]. We observed that RCN accounted for 3.12% of all cases of ARF in this study. The incidence of RCN decreased to 1.6% in 1995–2005 from 6.7% of total cases of ARF in the present study in 1984–1994. Liano and Pascual [12] observed RCN in only one case (0.13%) among 46 patients with renal biopsy in their series of 748 cases of ARF [12]. Thus, in recent years (2000s), RCN is an extremely rare cause of ARF in Europe. These observations indicate that RCN incidence is still high in developing countries in comparison to Europe and North America. The higher incidence of RCN in developing countries, including India, is related mainly to ARF occurring during obstetric complication.

Obstetric complications are the most common (50–70%) causes of RCN and non-obstetric causes account for 20–30% of all cases of cortical necrosis [2,13–15]. Obstetric causes were responsible for RCN in 56% and 61% of cases in previous Indian studies [14,15]. Obstetric causes are still the most common causes of RCN and 56.2% of RCN was due to obstetric complications in present series. The incidence of RCN ranges from 10–30% of all cases of obstetric ARF. Obstetric causes accounted for 9% of cases of cortical necrosis in patients with obstetric ARF in Pakistan [16]. The overall incidence of RCN in obstetric ARF was 25% in our previous series [14]. The present series reported the incidence of RCN in obstetric ARF was 15.2%. The incidence of RCN has declined from 17% in 1982–1991 to 2.4% in 1992–2002 in obstetric ARF in our recent publication [17]. Septic abortion continued to be an important cause of RCN and endotoxin-mediated endothelial damage leads to vascular thrombosis and subsequent renal ischaemia in patients with septic abortion. RCN in placental abruption may be due to a combination of a hypercoagulable state, endothelial injury and intravascular thrombosis. Abruptio placenta is the most common obstetric cause of RCN accounting for 50–60% of cases in developed countries [18,19]. However, RCN is very rare following septic abortion in developed countries but a common obstetric cause of RCN in India [15,20,21]. The reasons for this discrepancy is the fact that abortions are commonly conducted by untrained persons under unhygienic settings accounting for a higher incidence of septic abortion and sepsis-related complication.
Non-obstetric causes of RCN include extensive burns, snake bite, sepsis, HUS, pancreatitis, dehydration in infancy and childhood and organophosphorous poisoning [22–26]. Sepsis with septic shock is the most common (30–40%) non-obstetric cause of RCN [14,15]. HUS was the most common (72%) non-obstetric cause of RCN in the present series. In a recent review, 28 patients of RCN in English literature after 1980 were analysed to investigate the changes in its clinical feature in comparison with reported data before 1980 from two large centres in France (F) and India (I). Obstetric causes decreased from 68% (F) and 71% (I) before 1980 to 28% after 1980, whereas non-obstetric causes increased from 32% (F) and 29% (I) to 72% after 1980. Among the non-obstetric causes of RCN, the leading cause was sepsis in 4 out of 12 patients (F) and snakebite for 6 out of 14 patients (I) before 1980, but, in contrast, drugs in 4 of 21 patients after 1980 [27]. Non-obstetric causes contribute to RCN in 19.9% of cases in an autopsy series of 131 patients with post-surgical ARF in Japan [28].

We have observed obstetric and non-obstetric causes of cortical necrosis in 56.2% and 43.8% of cases, respectively. There is a slight increasing trend in non-obstetric causes of RCN, but, still obstetric causes remain the main cause of RCN in Indian patients. The reasons for higher incidence of RCN in HUS are not clear but could be due to higher incidence of gastrointestinal infection. Endotoxin-mediated endothelial damage leading to vascular thrombosis is an additional mechanism of reduced renal perfusion in haemolytic uraemic syndrome.

Two histological patterns of RCN were observed in the present study; diffuse 41 (72%) and patchy in 16 (28%). Thirty (52.6%) patients died during the acute phase of the illness. Causes of death included; severe uraemia, septicemia, pulmonary oedema, gastrointestinal haemorrhage and hyperkalaemia (Figure 3). The mortality was higher in the obstetric group as compared with non-obstetric group. In untreated patients the mortality rate exceeds 50%. Early initiation of dialysis significantly diminished this rate. Chronic renal failure occurred in 30–50% of patients requiring dialysis and transplantation. We observed 11 (19.2%) patients with patchy cortical necrosis who had partial recovery of renal function and were dialysis independent. The remaining 16 (28%) patients progressed to end-stage renal disease (ESRD). Progression to ESRD was seen in a higher number of cases in the second period 10 (47.6%) in comparison with 6 (16.6%) patients who progressed to ESRD in the first period, and the difference was statistically significant (P < 0.05). The lower (16.6%) progression to ESRD in the first period was due to high (72%) mortality during this period. The incidence of RCN is decreasing in developing countries. The incidence of RCN was 6–8% in other previous studies [4–6]. However, the incidence was found to be 3.4% in a recent study from Chandigarh [11]. We noted RCN accounts for 4.6% of total cases of ARF in our previous study [10]. Our recent study revealed, incidence of RCN in obstetric ARF has decreased to 2.4% in 1992–2002 from 17% in 1982–1991 [17]. A similar trend was observed in our present study as well. We observed a decline in the incidence of RCN from 6.7% in 1984–1994 to 1.6% in 1995–2005 of all cases of ARF. This change is mostly due to a decline in incidence of septic abortion. Legalization of abortion, public awareness and improved health services are

![Fig. 3. Causes of mortality in patients with RCN (n = 30).](image-url)

### Table 2. Comparative data: incidence and outcome of patients with renal cortical necrosis of all cases of acute renal failure in two 11-year periods; 1984–1994 and 1995–2005

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Study periods</th>
<th>Statistical analysis</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Total ARF cases</td>
<td>536</td>
<td>1286</td>
<td>2.17</td>
</tr>
<tr>
<td>Obstetric ARF</td>
<td>76 (14%)</td>
<td>134 (10.4%)</td>
<td>4.47</td>
</tr>
<tr>
<td>Total number of cortical necrosis</td>
<td>36 (6.7%)</td>
<td>21 (1.6%)</td>
<td>4.41</td>
</tr>
<tr>
<td>Obstetric RCN</td>
<td>25 (4.7%)</td>
<td>07 (0.5%)</td>
<td>1.42</td>
</tr>
<tr>
<td>Non-obstetric RCN</td>
<td>11 (2.0%)</td>
<td>14 (1.0%)</td>
<td></td>
</tr>
<tr>
<td>Outcome of RCN (n = 36)</td>
<td>(n = 21)</td>
<td></td>
<td>Chi square test</td>
</tr>
<tr>
<td>Mortality</td>
<td>26 (72%)</td>
<td>04 (19%)</td>
<td>12.99</td>
</tr>
<tr>
<td>Progression to ESRD</td>
<td>06 (16.6%)</td>
<td>10 (47.6%)</td>
<td>4.85</td>
</tr>
<tr>
<td>Partial recovery of renal function</td>
<td>04 (11.1%)</td>
<td>07 (33.3%)</td>
<td>2.90</td>
</tr>
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*aWith continuity correction factor.*
other reasons for this improved scenario. Mortality had also decreased from 72% in 1984–1994 to 19% in 1995–2005, due to better availability of dialysis and improved medical facilities.

In conclusion, RCN is an uncommon but a catastrophic entity with high mortality. Its incidence and severity were higher in developing countries in previous studies, mostly occurring due to pregnancy-related complications. With improved health care, the incidence and severity of RCN is decreasing in developing countries also, as illustrated in this study. We observed RCN accounts for 3% of all cases of ARF in the present series. The prognosis of RCN had improved in recent years with increased patient survival and better renal outcome.

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Conflict of interest statement. None declared.

References


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