Epidemiology of Acute Kidney Injury

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Background and objectives: The worldwide incidence of acute kidney injury is poorly known because of underreporting, regional disparities, and differences in definition and case mix. New definitions call for revision of the problem with unified criteria.

Design, setting, participants, & measurements: This article reports on the research recommendations of an international multidisciplinary committee, assembled to define a research agenda on acute kidney injury epidemiology using a modified three-step Delphi process.

Results: Knowledge of incidence and risk factors is crucial because it drives local and international efforts on detection and treatment. Also, notable differences exist between developing and developed countries: Incidence seems higher in the former, but underreporting compounded by age and gender disparities makes available data unreliable. In developing countries, incidence varies seasonally; incidence peaks cause critical shortages in medical and nursing personnel. Finally, in developing countries, lack of systematic evaluation of the role of falciparum malaria, obstetric mechanisms, and hemolytic uremic syndrome on acute kidney injury hampers efforts to prevent acute kidney injury.

Conclusions: The committee concluded that epidemiologic studies should include (1) prospective out- and inpatient studies that measure incidence of community and hospital acute kidney injury and post–acute kidney injury chronic kidney disease; (2) incidence measurements during seasonal peaks in developing and developed countries; and (3) whenever available, use of reliable existing administrative or institutional databases. Epidemiologic studies using standardized definitions in community and institutional settings in developing and underdeveloped countries are essential first steps to achieving early detection and intervention and improved patient outcomes.


The incidence rate of acute kidney injury (AKI) around the world is not well known (1–3). Recent studies in the United States (4,5) and Spain (6) have shown incidences varying between an average of 23.8 cases per 1000 discharges (4) with an 11% yearly increase between 1992 and 2001, to an increase from 61 to 288 per 100,000 population between 1988 and 2002 (5). More recently, Ali et al. (7) reported a high incidence of 1811 cases of AKI per million population during 2003. The relatively wide disparity in reported incidence rates and the increasing frequency of the condition raise concerns as to the real magnitude of the problem. In addition to a real increase in worldwide incidence, large differences in the definition of AKI and case mix likely underlie such differences.

It is recognized that the epidemiology of AKI in developing countries differs from that of the developed world in many important ways (8–16). Whereas in developed regions elderly patients predominate (4,5), in developing countries, AKI is a disease of the young (14,17,18) and children (19,20), in whom volume-responsive “prerenal” mechanisms are common (21–24). Although overall mortality seems to be lower than in developed countries (25–28), this finding is not true across all age groups: In these regions, AKI affects predominantly the young and children and mortality is high (29,30).

The difficulties of defining the incidence of AKI are especially notable when one searches for data on developing countries (8,13,15,16,25,31–33), the place of residence of more than 50% of the world’s population. No nationwide collection systems are available, and data from isolated centers are not based on the...
current AKI definition. Reports from Kuwait (8) reported an incidence of 4.1 per 100,000 population per year; Anochie et al. (31) in Nigeria reported an incidence of 11.7 cases of AKI per year in children in a hospital that serves more than 1 million children; in a tertiary care center in north India, the reported incidence was 20 cases per 1000 pediatric admissions (29). Among adult patients from South Africa, Seedat (25,34) reported an incidence of 20 cases per year per million population; in Brazil, Noronha et al. (10) reported an incidence of 7.9 cases per 1000 hospital admissions, and in North India, Jha and Chugh (33) reported a yearly incidence of 6.4 per 1000 admissions.

New definitions of AKI (35–37) make it again necessary to revisit this issue with unified criteria. Such new measurements will help us to understand the magnitude of the problem and enable meaningful comparisons between different centers and geographic regions. Previous articles have reviewed the status of this rapidly changing field (1–3). A recent systematic review described the similarities and differences in incidence, cause, pathophysiology, and public health implications of AKI in developed and developing regions (16). This article aims to build on such a review of existing knowledge and present a research agenda to begin to address the multiple areas of uncertainty in the epidemiology of AKI. This is the first time a multidisciplinary group including representatives from the main national and international societies of nephrology and critical care gathers to elaborate such a research agenda. The group understands that only by obtaining accurate knowledge on the epidemiology of AKI using contemporary diagnostic criteria can the problem acquire the necessary visibility that will enable the development of new initiatives. Such initiatives will be essential to move us forward in the field, decrease the worldwide incidence of AKI, and improve patient outcomes (36,38).

As long as AKI remains underreported, it will not be addressed properly. In developing countries, the most common causes of AKI are frequently associated with volume-responsive “prerenal” (39,40), obstetric (41), infectious (42,43), or toxic (25,44) mechanisms; thus, inexpensive, simple interventions such as education on oral rehydration (29,45), improved cross-cultural interaction with traditional healers (46), change in obstetric management policies (47,48), or management of infection (49) may result in a dramatic reduction in the incidence and severity of AKI (29,42,45–49). Given that in developing countries the costs of renal replacement therapies are prohibitively high (17,50–52), prevention is often the only realistic way to decrease its severe impact on morbidity and mortality. Although inexpensive, such interventions will not be carried on until the problem reaches political visibility and achieves institutional and organizational support (16).

**Materials and Methods**

For the purposes of defining a research agenda in the context of the epidemiology of AKI, we used a modified Delphi process. This is described in detail by Kellum et al. (53) in this issue. Briefly, the three-step modified Delphi procedure included a literature review phase, focused group interactions with presentations to the entire committee, and a final ranking phase during which the research agenda was developed.

**Literature Review and Synthesis**

We conducted a systematic review of the literature using the following databases: Medline (1966 through August 2006), EMBASE (1980 through 2006, week 36), CINAHL (1982 through August 2006), and PubMed. Articles in any language were considered. The purpose of the review was to identify key unanswered questions. A secure internet Web site was set up with FTP capability; group members were able to upload and download full-text articles, and through a number of iterative steps, a series of clinical questions were developed.

**Work Group Deliberations**

After reviewing the literature and establishing a global perspective on the problem, discussions were undertaken within the work group regarding key knowledge gaps and recommendations for research that would improve the understanding of AKI worldwide. An organizational framework for AKI was introduced and discussed (Figure 1). In addition, recognizing that AKI commonly precedes or aggravates chronic kidney disease (CKD) (20,54–60), a schematic view of the natural history of AKI was developed (Figure 2).

**Results**

**Global Perspectives**

Local conditions in developing countries make underreporting an important problem (1,16). It is improbable that incidence rates are so much lower in these regions than in developed countries. The most likely explanation for the seemingly lower incidence of AKI is that the majority of patients who develop AKI never make it to large reporting centers: The condition is underrecognized, distances are enormous, and the costs of transportation and lost wages are prohibitive (3). Delayed referral as a result of transportation difficulties and traditional cultural mores is still a formidable problem in many regions of the world (61) associated with significantly worse outcomes, as seen among children with hemolytic uremic syndrome in India (30).

Gender disparities in seeking medical attention make available reports even more unreliable. Thus, in certain regions in Africa and India, boys are more than twice as likely as girls to be taken by their parents to see medical personnel (62–66). Gender disparity is also expressed in the development of AKI after septic abortion (41,67). In some African countries, the problem has unfortunately worsened (41) despite nationwide efforts.

In developing countries—even at large centers—the availability of medical and nursing personnel is limited. This limitation becomes even more critical during seasonal variations in incidence (10,68–70). For example, during the monsoon season in Southeast Asia, the incidence of AKI may increase by 18 to 24% as a result of the increase in new cases of malaria, leptospirosis, acute gastroenteritis, and dysentery (71).

The causes and risk factors for AKI in developing countries may be different from those in developed countries. Although prerenal or toxic mechanisms predominate, specific etiologies are important.
The incidence of acute glomerulonephritis, both primary and secondary to infectious diseases appears to be higher than in developed countries. Thus, in south-east Anatolia, Turkey, acute glomerulonephritis causes more than 60% of childhood cases of AKI (72), and is an important cause of AKI in northern Africa (73–75). Potential reasons are multiple, including access to care (leading to late and therefore severe presentation), diagnostic testing capabilities and perhaps a true incidence difference. This is an important research question that warrants further study.

Malaria represents an especially important problem (16). There is an upsurge in worldwide malarial incidence (76,77). In India, for example, the overall yearly incidence is 13 to 17.8% of malarial cases (43). Incidence is increasing in Africa, India, Thailand, and New Guinea (42). As its worldwide incidence increases, so are the complications of severe falciparum malaria, including AKI (78). Each year, 300 million people contract the disease, which will be responsible for more than 1 million yearly deaths in Africa alone (49,77). It is estimated that in 1% of cases (3000,000/yr), a combination of parasite and host factors will lead to severe malaria, jaundice, and AKI (42,78), a complication associated with 45% mortality (78); in areas of endemic malaria, the incidence of AKI may be >4% of malarial cases (42). Worldwide, the incidence of AKI as a result of malaria varies between 0.6 and 60% of malarial cases, depending on the region (43). Early intervention, including appropriate antimalarial treatment and renal replacement therapy, is associated with improved survival and recovery of kidney function among patients with AKI as a result of severe falciparum malaria (79,80).

Specific Problems in Children

Although the majority of causes of AKI in children around the world are secondary to volume-responsive mechanisms, including acute diarrheal losses and renal hypoperfusion after major surgery and secondary to systemic sepsis (81–83), other conditions have shown an increased frequency in certain regions of the world. Thus, hemolytic uremic syndrome (HUS) is the chief cause of CKD and ESRD in children in Argentina (84) and in northern India (85), where it has increased in frequency in comparison with previous surveys (45). Whereas in Argentina the mortality associated with HUS has decreased from 10 to 3% (84), in India, it remains high (up to 59% [29]), attributed often to late referral of patients (30). An additional complication to longitudinal incidence comparisons is that some diseases virtually did not exist a few years ago; thus, HUS was very uncommon in south and southeast Asia before the 1970s but has since then become one of the most important causes of AKI in children of that region (29). Follow-up studies of patients suggest that of the patients who have AKI and are successfully discharged from the hospital, a significant proportion may show features of CKD, including low GFR, hypertension, and proteinuria (20,84).

The Elderly and Complex Patients

Although it is widely known that the elderly and those with multiple medical conditions are at increased risk for AKI (4,5,86), the measurement of this risk is inaccurate, especially in outpatient situations. It remains unclear whether the underlying condition(s) increases susceptibility or whether those patients are more likely to be exposed to important initiating factors for AKI.
Research Recommendations

Key research studies to evaluate incidence and risk factors are crucial. Knowledge of the magnitude of the problem will drive local and international efforts to detect and treat the problem as early as possible. The scarcity or absence of data makes it unlikely that the problem will be addressed by local, regional, and worldwide organizations such as the Pan American Health Organization and the World Health Organization in a strong, consistent manner. Accurate knowledge of the epidemiology of AKI in developing countries will have powerful preventive and treatment effects (18,29,30,45,80,87); conversely, complex technical questions on renal replacement therapies may, for the time being, largely remain less relevant to this population (51,52).

Epidemiology of AKI in Developing and Developed Countries

There is a need for a variety of epidemiologic studies to acquire new knowledge about the incidence of AKI. Although data collected from surveys, administrative data sets, post hoc analysis of clinical trials, or review of existing laboratory or clinical databases have important methodologic limitations, it is clear that without attempts to quantify the true burden of illness using standardized definitions, improved understanding and outcomes will not be possible.

Establishing the True Incidence in Different Locations. Studies using the new definition of AKI can be instrumented in a prospective manner, such as measuring the incidence of AKI in emergency departments to measure community-acquired AKI and among hospital inpatients to measure hospital and intensive care unit–acquired AKI. Such measurements can then be followed up longitudinally for 3, 6, and 12 mo to ascertain the natural history of the problem and to measure the importance of AKI as a cause of CKD (see Figure 2). In developing countries, where community-acquired AKI occurs in the rural setting and rarely reaches the hospital, different regional data collection techniques will be necessary to ensure accurate measurement of incidence.

Unique situations that may facilitate knowledge acquisition include data collection during periods of presumed increased incidence, such as during monsoon season in Southeast Asia (68,70) or the rainy season in South America (10,88). If local resources are used, then such studies would not be costly and could be obtained in a short period of time. Local innovations in this regard would enable acquisition of data at small cost.

Establishing True Incidence in Different Locations/Situations. In developed countries, use of currently existing administrative or institution databases whenever available will help to establish the prevalence of abnormal kidney function at the time of admission to hospitals or emergency departments and the occurrence of changes in renal function during hospitalization. Collecting information about populations at risk (e.g., elderly patients in nursing homes during influenza season or before and after vaccination) would also enable more precise estimates of the burden of illness. Such databases are rarely available (32,41,89) in developing countries.

Conclusions

AKI is a worsening problem, but its true incidence is unknown. From a worldwide perspective, there is a clear need to understand the epidemiology of AKI more accurately. Use of standardized definitions and descriptions of existing at-risk and high-risk populations, both in community and institutional settings in developing and underdeveloped countries, are the first steps to improve outcomes.

Disclosures

None.

References

44. Luyckx VA, Steenkamp V, Stewart MJ: Acute renal failure associated with the use of traditional folk remedies in South Africa. Ren Fail 27: 35–43, 2005


