Targeted Review of the Epidemiology and Burden of Anemia in Chronic Kidney Disease

Poster #191

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INTRODUCTION

- Anemia is a common complication in patients with chronic kidney disease (CKD); it is associated with progressive disease severity, poor quality of life (QoL), and increased morbidity and mortality[1-3]
- While the prevalence of anemia is high, there are few publications available summarizing the contemporary epidemiologic burden of anemia in patients
- The objectives were to review the existing evidence regarding the epidemiologic burden associated with anemia in CKD, including natural history of disease, incidence, prevalence, mortality, and disease severity

METHODS

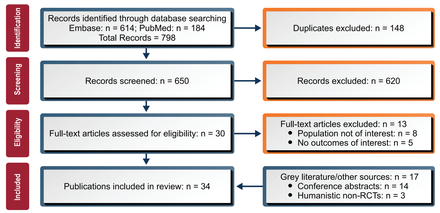
- A targeted literature review was conducted to identify studies reporting on the epidemiological burden of anemia in patients with CKD published between January 1, 2013 and June 27, 2018
- Literature searches using key terms for CKD, anemia and the outcomes and study designs of interest were conducted in the electronic databases Embase and PubMed
  - Along with grey literature consisting of the last two last two conference proceedings from the Academy of Managed Care Pharmacy (AMCP), American Society of Nephrology (ASN), European Renal Association-European Dialysis and Transplant Association (ERA-EDTA), International Society of Nephrology (ISN) - World Congress of Nephrology, International Society of Pharmacoeconomics and Outcomes Research (ISPOR)
- Predetermined eligibility criteria for article selection included the following: participants diagnosed with anemia in CKD, aged 18 years or older, outcome of interest, US-based, and published in English in the last five years (**Table 1**)
- PRISMA guidelines and the Guidance on the Conduct of Narrative Synthesis in Systematic Reviews were followed (**Figure 1**); study procedures were outlined in a study protocol

Table 1. Eligibility criteria for study inclusion

PICO-T	Epidemiological Outcomes Review
Population	Adults (aged ≥18 years) with CKD-related anemia
Interventions	NA
Comparators	NA
Outcomes	Natural history of disease Disease severity Incidence Prevalence Morbidity Mortality
Timeframe	2013–2018
Study design	Cohort studies (retrospective or prospective) Cross-sectional studies Case-control studies Systematic Literature Reviews (for reference-checking only)
Geographic region	US
Language of publication	English
Other limits	Humans

CKD: Chronic kidney disease.

Figure 1. PRISMA Flow Diagram: targeted review of epidemiology and burden in CKD-anemia



RESULTS

Figure 2. Study characteristics

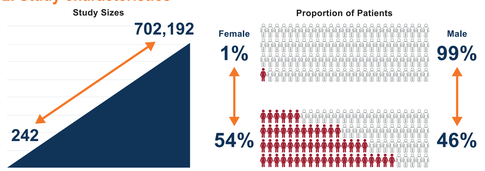


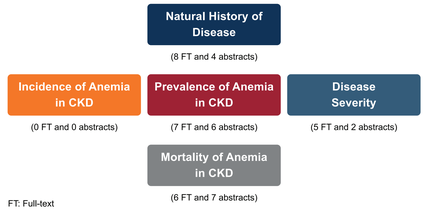
Figure 3. Study designs

- The electronic search strategy retrieved 667 unique publications
- 34 articles were included in the qualitative analysis
  - Study designs included retrospective observational studies (n=25), prospective (n=8), and one study using cross-sectional data (**Figure 3**)
  - Studies primarily covered outcomes related to treatment patterns and natural history (**Figure 4**)
  - Notably, some studies were reported via multiple publications
- Study sizes ranged from 242 to 702,192 participants, while the proportion of female patients ranged between 1% and 54%
  - Patient populations studied (n=study size):
    - **NDD**, n=14 (pre-ESRD, n=1; Stage 2-4, n=3; Stage 2-5 [non-dial], n=1; Stage 3-4, n=1; Stage 3-5 (n=8) NR, n=1 (stage[s] not reported)
    - **DD**, n=16 (all Stage 5 [ESRD])
    - **DD/NDD**, n=3 (not reported, n=2; Stage 1-5, n=1)

NDD: Non-dialysis dependent, ESRD: end-stage renal disease (ESRD), NR: Not Reported, DD: Dialysis-dependent

RESULTS

Figure 4. Eligible studies across outcomes of interest



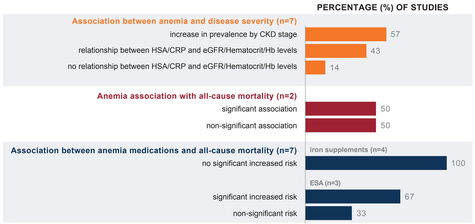
Outcomes of interest (Figure 4)

- Overall patient populations were heterogeneous in terms of size, gender, age, dialysis status and CKD stage and the study designs used varied
- Prevalence varied greatly (range: 15%–69%) in 10 studies of diverse populations; and they were closely associated with older age and disease progression
- No studies reported on incidence of anemia
- Several studies provided evidence that females (n=4), increased age (n=5), and non-Caucasian race (n=4) were significant predictors of anemia with CKD; Furthermore, a previous history of anemia (n=3), low education (n=1), and altitude (n=1) were also predictors of the odds of having anemia with CKD
- Three studies reported an exact percentage of anemia prevalence associated with disease severity. The prevalence of anemia among Stages was:

Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
8.4%	12.2%	17.4%–43.9%	41.3%–64.0%	53.4%–53.9%

- There were 13 studies that reported information on the relationship between anemia in CKD, all-cause mortality, cardiovascular death, or composite cardiovascular events
- Seven studies included patients with ESRD, two studies in Stages 3-5, one in stages 2-5, while the rest did not report CKD severity and the time span of reported results was pretty wide ranging from 1999–2017
- Four studies reported higher all-cause mortality (range: 15%–35%) and higher mortality; of the two studies exploring associations between anemia and mortality, one reported a non-significant association
- A total of 9 studies examined the association of all-cause mortality with anemia medications, including iron supplements (n=4), erythropoietin-stimulating agents (n=4) or both (n=1) and reported mixed findings for the association of mortality outcomes with anemia treatments (ESAs and/or iron supplements)

Figure 5. Associations between anemia and disease severity, all-cause mortality



HSA =hepatocyte specific antigen; CKD= chronic kidney disease; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; Hb= hemoglobin; ESA = Erythropoiesis-stimulating agents

CONCLUSIONS

- Given the sparse data, epidemiologic burden remains a gap in peer-reviewed literature, especially with respect to incidence of anemia in CKD in the US over the last five years.
- Limitations of this review include data gaps and selective methods which led to evidence that was identified in a targeted manner.
  - Review was limited to evidence available in the past five years (January 1, 2013 to June 27, 2018) and therefore, the findings overlook key studies known to have been published prior to the search cut-off dates.
  - Evaluation of the individual study quality were not performed for included studies thus study quality may also be heterogenous.
  - Lastly, studies were limited to those conducted in the US, which may limit applicability and transferability of the findings to other contexts and situations.
- This summary was on heterogenous patient populations in terms of disease severity and designs of the studies.
- Findings demonstrate wide ranges of reported prevalence, evidence of association of CKD anemia and CKD severity but less information published relating to the relationship between mortality and anemia, and possible factors associated with natural history of disease.

References

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Disclosures

MA, AB, and AE are employees of Evidera. SM and MS are employees of Otsuka Pharmaceutical Development & Commercialization, Inc. GS, Ana B and YF are employees of Akebia Therapeutics, Inc., where AB was employed during the time the research was completed.

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