Is Cystic Fibrosis Contributing Significantly to Infant Mortality Rate in India?

Cystic fibrosis is a life-limiting, genetic disease. Over the last 80 years, predicted life expectancy of affected individuals has improved from less than one year to the fifth decade of life, largely due to early initiation of aggressive supportive treatment [1]. In India, diagnosis of cystic fibrosis is made at an average age of 4.5 to 6.5 years and is associated with high mortality in childhood [2-4].

Over the last decade, at a tertiary care center in southern India, blood samples for *CFTR* mutation analysis were stored, with the permission of the parents after genetic counseling, for all critically ill young infant in the PICU with a presumptive diagnosis.

In this retrospective study, we reviewed the mortality data of young infants between 1 and 6 months of age during 3.5 years period from July, 2018. Institutional review board approval was obtained. There were total 81 young infant deaths. The diagnosis of cystic fibrosis was confirmed posthumously in six infants (mean age 3.7 month) by *CFTR* mutation analysis on stored blood. The clinical diagnosis at the time of death were severe community-acquired pneumonia in five and intracranial bleed in the sixth baby. Notably, all had failure to thrive, anemia (mean hemoglobin 6.9 g/dL, range 4.7-10.6g/dL) and hypo-albuminemia (mean serum albumin 1.9 g/dL, range 1.5 - 2.9g/dL). During the study period, cystic fibrosis was found to be the fourth most common cause of death in this age group, after cardiac disease (48%), pneumonia/sepsis (25%) and other congenital conditions (19%).

We believe, that these undiagnosed cystic fibrosis cases may be contributing to the infant mortality, especially in tertiary care centers located in geographic areas where *CFTR* mutation carrier frequency is high and endogamous marriages are practiced. Infant deaths due to cystic fibrosis can be prevented with timely genetic counseling, early diagnosis and initiation of supportive treatment. Accurate data on incidence and genetic profile of cystic fibrosis in India need to be generated to understand the true burden of this disease and the related infant mortality.

Pediatricians in India should have high index of suspicion for cystic fibrosis clinically. It should be suspected if there are two or more features of recurrent pneumonia, oily stools, history of consanguinity, history of sibling death, hypochloremic hypo-kalemic metabolic alkalosis and isolation of pseudomonas from respiratory specimens. With a presumptive diagnosis of cystic fibrosis, treatment can be started even without sweat chloride or genetic tests and confirmation may be done when feasible.

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Referencing Made Easy: Handling Reference Management Softwares

As a long-time user of the Zotero reference management system, I read with interest the recent article on reference management softwares [1]. I consider reference management systems (RMS) to be one of the most useful tools that have been brought for writers in the last two decades. Developments in the RMS field have been quite dynamic in recent years and therefore, I would like to underscore additional points regarding them.

The authors stated in Table I that Zotero does not allow reference sharing. I have been using groups in Zotero (*https://www.zotero.org/groups/)* for reference sharing for many years. Second, the authors stated that users of other RMS than Endnote, Mendeley and Citavi cannot use annotations as sticky notes and highlight texts in PDFs directly in RMS. This feature has been added to Zotero since version 6 was released in 2021 (*https://www.zotero.org/blog/zotero-6/*).

The authors have also stated that each author needs to meet the specific citation requirements of the journal. It is worth noting that many journals and international publishers do not