

DEHYDRATION IN THE ELDERLY: A REVIEW FOCUSED ON ECONOMIC BURDEN

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Abstract: *Background:* Dehydration is the most common fluid and electrolyte problem among elderly patients. It is reported to be widely prevalent and costly to individuals and to the health care system. The purpose of this review is to summarize the literature on the economic burden of dehydration in the elderly. *Method:* A comprehensive search of several databases from database inception to November 2013, only in English language, was conducted. The databases included Pubmed and ISI Web of Science. The search terms «dehydration» / “hyponatremia” / “hypernatremia” AND «cost» AND «elderly» were used to search for comparative studies of the economic burden of dehydration. A total of 15 papers were identified. *Results:* Dehydration in the elderly is an independent factor of higher health care expenditures. It is directly associated with an increase in hospital mortality, as well as with an increase in the utilization of ICU, short and long term care facilities, readmission rates and hospital resources, especially among those with moderate to severe hyponatremia. *Conclusions:* Dehydration represents a potential target for intervention to reduce healthcare expenditures and improve patients’ quality of life.

Key words: Dehydration, economic costs, hospitalized patients, elderly.

Introduction

Declining birth rates and increased life expectancy have substantially raised the proportion of elderly people in the population and the total number of older people around the world and these trends are expected to continue (1). Worldwide, those aged 60 years and over are the fastest growing segment of the population and those over 80 years are the fastest growing group (1).

The elderly population has a high rate of chronic illness (2) and is more vulnerable to disease. People aged 65 and over have more hospital stays than any other group. Ageing populations will therefore place even greater demands on social and health services around the world (1).

Dehydration is the most common electrolyte disorder among elderly patients. It is widely prevalent and costly to individuals and to the health care system (3). According to U. S. statistics, \$1.36 billion was spent in 1996 to treat hospitalized elderly patients with dehydration as their primary diagnosis (4). Particularly dehydration often leads to poor health and medical outcomes; increased hospitalization, and increased usage of long term care (LTC) facilities. It is associated with significantly longer stays in rehabilitation settings and contributes to the development of chronic diseases (5). Therefore because of its high incidence of cases among the elderly, small increases in its prevalence can translate to substantial impacts at the population-level. The present article is a review of the literature of dehydration among the hospitalized elderly population, with a main focus on economic burden.

Methods

Search strategies

A comprehensive search of several databases from database inception to November 2013, only in English language, was conducted. The databases included Pubmed and ISI Web of Science. The search terms «dehydration» / “hyponatremia” / “hypernatremia” AND «cost» AND «elderly» were used to search for comparative studies of the economic burden of dehydration.

Study selection

We considered all the empirical studies published in English language that evaluated the effect of dehydration on hospital outcomes of elderly patients diagnosed with dehydration. Studies were eligible if their cohort of patients had a mean age > 60 and if they reported medical outcomes other than mortality. They were reviewed and rated based on their relevance to cost of illness and the reliability of the estimates. Initial abstract screening excluded non-relevant studies or non-original studies. Full-text screening was then performed to assess eligibility. The total number of articles retrieved was 126. After a filtering process based on the text of the abstract, we kept 15 studies. Study characteristics and reported outcomes are described in Table 1.

Furthermore depression and loneliness usually observed in elderly patients have been identified as major contributors to inadequate fluid intake in hospital and nursing elderly residents. Term depression reflects symptoms such as sadness, lack of motivation, social isolation, and hopelessness (6).

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Dehydration as a medical problem

Dehydration in clinical practice, and especially long term care, is most often functionally considered as a loss of total body water content due to pathologic fluid losses, diminished fluid intake or a combination of both (7). However it is important to understand and distinguish the body's three forms of water depletion; hypertonic, isotonic and hypotonic (different serum sodium levels) (8) in order to address and underline the causes in a timely and appropriate manner.

Many studies looking at the clinical outcomes of dehydration have shown that decreased fluid intake has a direct impact on individuals' health status. Dehydration has been proved to be a major risk factor in the development of many diseases such as stone disease (9, 10) or it appears as a comorbid condition of multiple diseases such as mitral valve prolapse and salivary dysfunction (11, 12) certain types of cancers (12-14), pulmonary diseases (15), heart failure (16), physical impairment (17-21) contributing to their deterioration (22)

Dehydration is not only widespread among the elderly, but also an independent predictor of mortality. A number of studies have reported mortality rates associated with hypernatremia greater than 40% (23-25) and are commonly related to the underlying disease processes (24, 25). In a cohort of 4123 elderly patients, Terzian et al (26) studied the relationship between hyponatremia at the time of hospital admission and treatment outcomes. After controlling for different confounders hyponatremia was a significant independent predictor of mortality. In more recent studies such as the one by Wald et al. (27) patients diagnosed with hyponatremia (<135 mmo/L) had a risk of in-hospital mortality as high as 47%, and that risk was doubled for patients with a serum sodium concentration between 125 and 129 mmo/L.

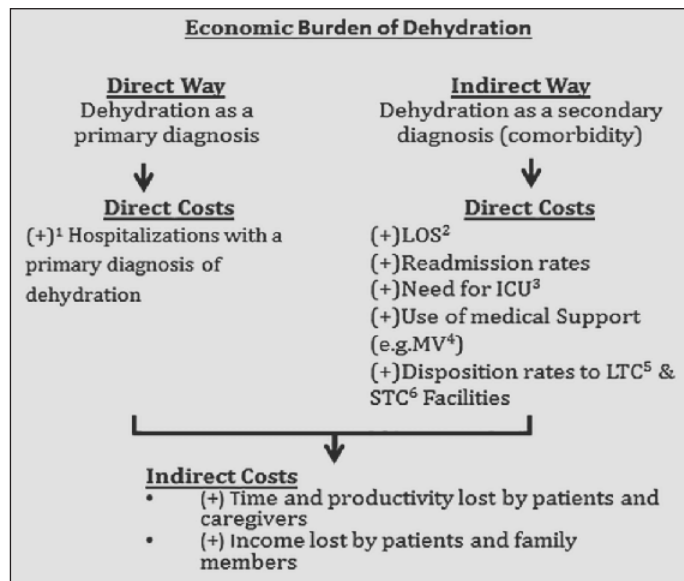
Increasing age is a strong independent risk factor for both hypo- and hypernatremia (28). The concept of progressive intermittent frailty almost ensures that the elderly will go through periods of illness with associated dehydration (29). The reasons of elderly being exposed to higher risk of dehydration are well known and documented in the literature.

Firstly water and salt homeostasis are affected by a variety of age related factors (30, 31). As one ages, there is less total body water due to a decrease in lean body mass and an increase in percentage of body fat (32, 33). Moreover kidneys of elderly people present structural as well functional changes (34,35) leading to the development of hyponatremia. Hyponatremia in turn increases the risk of other illnesses (e.g. disorientation, coma etc.) (36).

In addition thirst sensation is lessened with age (32). Findings consistently support the conclusion that the elderly do not feel as thirsty as younger persons following water deprivation and subsequently do not drink enough to rehydrate themselves (7, 37). Many elderly may also intentionally reduce their fluid intake to reduce incontinence, which has been found as a risk factor for significantly lower fluid intake for avoiding

humiliation (38, 39).

Figure 1
Economic Burden of Dehydration



1. Increase/ 2. Length of Stay/ 3. Intensive Care Unit/ 4. Mechanical Ventilation/ 5. Long Term Care/ 6. Short Term Care

Dehydration in the elderly

Another factor that contributes to the prevalence of dehydration in elderly people is their higher rate of chronic illness (2) which can disrupt the body's ability to balance and manage fluids and electrolytes (40, 41). For example persons with diabetes (42) or neurological and neurosurgical diseases are (8, 43, 44), cognitively impaired (40) are particularly at risk for dehydration. However the relationship of delirium and dehydration is complex, because each may contribute to the other in a vicious cycle. Some elderly people simply do not know how much fluid they need or do not remember to ask for it because they are cognitively impaired (40) but dehydration can itself contribute to impaired mental function, which may then make the sufferer forget to drink, and so on (8).

Moreover, multiple diseases such as cardiac glycosides (45), furosemide (24), laxatives (46), and dilating suppresses vasopressin release (32) usually found in elderly are combined with intensive drug consumption which not surprisingly has untoward side effects on water and electrolyte balances of individuals. Additionally dehydration has also been associated with malnutrition (47), resulting in reduction of secondary thirst as food consumption declines. Another hypothesis suggests that aging is associated with changes in satiation that hinder adequate rehydration in response to hyperosmolarity (48) and swallowing difficulty (6).

Finally depression and loneliness usually observed in elderly patients (especially in nursing home patients) have been identified as major contributors to inadequate fluid intake in

Table 1
Characteristics of the Eligible Studies

Ref. No.	First Author, Year (Country)	Number of patients (n)	Inclusion criteria	Definition of dehydration	Prevalence of dehydration (%)	Mean Age (years)	Years of patient cohort	Single (S)/ Multicentre (M)	Setting	Data source	Mortality (in 31-360 days)	LOS (days)	Clinical outcomes Readmission rates (%) Admitted to ICU (%)	Average costs per patient
37	Warren et al, 1994 (US)	731,695	All Medicare beneficiaries hospitalized older than 64 years	ICD-9-CM: 276.5	65=<	1991	M	Hospital	MEDPAR	17.4% (in 30 days); 30.6% (in 31-360 days)			2,942 (\$) for cases with principal diagnosis of dehydration	
62	Mukand et al, 2003	39	Prospective pilot study with Orthopedic Patients	prerenal azotemia: BUN / Creatine ratio>=20 orthostatic hypotension: SBP<=15 ICD-9-CM: 276.5	53.80% 46.20%	78	2004-2005	S	Hospital	HD		12.9 vs 9.4 13.7 vs 9.8		
49	Hong et al, 2004 (US)	31,077	Hospitalization episodes patients >= 65 years principal diagnosis of dehydration; discharged alive	SSIL<135 mmol/L	19.70%	74.1	2003-2004	M	Hospital	OPTI MIZE-HF	6.0 vs 3.2	6.4 vs 5.5		
68	Gheorghade et al, 2007(US)	48,612	Patients hospitalized with heart failure (CHF)	Hyponatremia: (SSL<135 mmol/L) Hypernatremia (SSV>145mmol/L)	0.80% 1.90%	64	1999-2005	M	Hospital	IHCIS				Annual medical costs: 19215(\$)/92.57(\$)/Annual inpatient costs: 10636(\$)/468(\$) Annual medical costs: 10972(\$)/92.57(\$)/Annual inpatient costs: 4734(\$)/3468(\$)
52	Shea et al, 2008 (US)	167,299	All hospitalized patients (any age)			59								
2	Wakefield et al, 2008 (France)	96 cases, 93 controls	Case control study. Cases are male patients with one of the three selected ICD-9 codes. Matched by age, ward location and admission month (within the same year)	ICD-9-CM: 276.0,276.1,276.5	0.55% (Hyponatremia accounted for 18.8% of dehydrated patients)	65	1995-2000	S	Hospital	HD	ns			
63	Zilberberg et al, 2008 (US)a	198,281	All patients hospitalized (any age). Objective: to estimate the prevalence of hyponatremia and the influence of admission hyponatremia on hospital costs and out	Hyponatremia SSL<135 mmol/L	5.50%	65.7	2004-2005	M	Hospital	Solucient's ACTracker	5.9 vs. 3.0	8.6 vs. 7.2	17.3 vs. 10.9	16502 vs 13558 (\$)

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62	Zilberberg et al, 2008 (US) ^b	7,965	comes Patients admitted with Pneumonia	SSL<135 mmol/L & ICD-9-CM: 276.5	8.20%	72.4	2004-2005	M	Hospital	Solucient's AC Tracker	7.6 VS 7.0	10 VS 6.3	7,086 VS 5,732 (\$)
71	Callahan et al, 2009 (US)	10,120	Retrospective cohort study all vs 13,066(\$)	SSL<129 mmol/L	20.20%	-	2004-2005	M	Hospital	HD	8 vs 6	32 vs 26	16,606 (\$)
27	Wald et al, 2010 (US)	53,236	Cohort study. All adult hospitalizations in which serum Sodium concentration was recorded were included. It compares Community acquired hyponatremia Hospital acquired hyponatremia: 37.9% 69 years	SSL<130-26 vs 22 SSL<135 mmol/L	14,266(\$ vs (any age) 13,066(\$) Community- acquired hyponatremia: 37.9%	66.7	2000-2007	S	Hospital	HD	3.4 vs 2.0 5.9 vs 5.2	9 vs 6	
67	Shorr et al, 2011 (US)	115,969	Community acquired hyponatremia hospital acquired hyponatremia Patients hospitalized with congestive heart failure (CHF)	Severe hyponatremia: SSL<130 mmol/L Hyponatremia: SSL<131-135 mmol/L Hyponatremia: SSL>145 mmol/L ICD-9-CM: 276.1	5.30% 15.90% 3.20%	75.4 74.3 76.9	2004-2005	M	Hospital	Care Fusion	7.6 vs 2.9 6.9 vs 5.4	11,109(\$ vs 9,192(\$) 10,033(\$ vs 9,192(\$) 9,418(\$ vs 9,192(\$) 15,281(\$ vs 13,439 (\$)	
58	Amin et al, 2012 (US)	558,815 cases and 558,815 controls	Retrospective study patients hospitalized, any age. Case control study. Comparisons of hospitalized hyponatremic (HN), primary or secondary versus non-HN patients	ICD-9-CM: 276.2	75.36	70	2007-2010	M	Hospital	Premier HD	7.7 vs 6.3 21.4 vs 5.0	13,339 vs 10,475 (\$). ICU Costs= 7,195 \$ vs 5,618\$	
60	Amin et al, 2013 (US)	25,855 cases and 25,855 controls	Patients hospitalized with heart failure any age. Case control study. Cases are hyponatremic patients, controls are non hyponatremic patients	ICD-9-CM: 276.2	75.36	70	2007-2011	M	Hospital	Premier HD	7.7 vs 6.3 21.4 vs 5.0	13,339 vs 10,475 (\$). ICU Costs= 7,195 \$ vs 5,618\$	
69	Rabino vitz et al, 2013 (US)	635	pulmonary hypertension	SSL<135 mmol/L	22.40%	66	2006-2008	S	Hospital	HD	Overall: 27% / HR=1.82	7.4 VS 6.3	
59	Turgutalp et al, 2013 (Turkey)	253	All elderly patients admitted in the ED department on 2010 were evaluated. It compares two groups of patients, 65-75 years and 75 and older	SSL<135 mmol/L	4.1% (65-74 years); 7.8% (75 years and older)	65<=	2010	S	ED	HD	9.56	58.6 Me dical support needed in 19.3% 76.9 Me dical support needed 35.9%	1,524.4 (\$)

*HCUP=Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample; *IHGIS=Integrated Health Care Information Services (IHGIS) National Managed Care Benchmark Database; *HD=HD (Hospital Database); *MEDPAR=Medicare Provider Analysis and Review (MEDPAR); *OPTIMIZE-HF registry=Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) registry; *SSL=Serum Sodium Level; *Whenever age of patients was reported for different groups we only reported the age of patient group diagnosed with dehydration; *ICD= International Statistical Classification of Diseases;

hospital and nursing elderly residents. Term depression reflects symptoms such as sadness, lack of motivation, social isolation, and hopelessness (8).

Prevalence of Dehydration among elderly

The evidence of dehydration among the elderly is well known and documented (49, 50). Dehydration affects a large number of elderly persons (51) and cases can only be expected to increase as the elderly come to make up an even larger segment of the population. Haveman-Nies et al (51) studied the fluid intake of elderly Europeans and found that fluid intake of elderly people varied between the towns of Europe and between men and women. A high percentage of the female population had a water intake below the cut-off value. Patients diagnosed with hyponatremia were more likely to be female in most of the studies (49, 52, 53).

Increasing age was a major factor in risk of admission with dehydration in most of the studies. For example Hong et al (49) using hospital discharge data from the Health Care Cost and Utilization Project (HCUP), found that more than half of the hospitalizations involving a principal diagnosis of dehydration were for individuals of at least 65 years of age. Warren et al (37) reported that patients 85 to 99 years of age were 6 times more likely to be hospitalized for dehydration than those 65 to 69 years of age. Similarly Curtze et al (54) found that hospitalization-required hyponatremia is more common in very elderly persons than in elderly (Table 1).

Furthermore hyponatremia has been reported to be almost 20% in older adults presenting to the emergency department (ED) (55) and it has also been observed in many hospital admissions of nursing home residents (8). Few older studies available on the prevalence of dehydration among the elderly suggested that those living in LTC facilities were twice as likely to be dehydrated (22%) as the acutely ill hospitalized elderly (11%)(56). More recent studies confirm these findings. Menten et al (57) found that dehydration events occurred in 31% of residents over 6 months and in two other studies, 34% of nursing home patients admitted to hospital were diagnosed with dehydration (39) and 84% of hypernatraemic patients developed this during admission to hospital while 16% were hypernatraemic on admission (23).

Economic Consequences

Enumeration of effects

Although the clinical consequences of dehydration in elderly are well documented, relatively little is known about the relationship between dehydration and medical costs. Hyponatremia among hospitalized and community elderly patients carries important clinical and economic implications. Whether it is present on admission, exacerbated after admission, or develops during hospitalization, it imparts a considerable burden on the consumption of healthcare resources (52, 58). It contributes to an increase

in hospitalizations (37, 49), admission to ICU (27, 58–60), readmission to the hospital (58) and dispositions to long term or short term care facilities (27, 61). It is evident that all these factors increase hospital costs through the increase in usage of hospital equipment, drugs, medical tests and procedures (59, 62, 63), need for hospital staff; doctors, nurses etc.

Cost types to be considered, sources and measures (direct and indirect costs)

Dehydration substantially increases the health care burden in a direct way, as a disease itself, or an indirect way as comorbidity of another disease. For example hospitalizations for dehydration can be assumed to be a direct predictor of healthcare costs. The number of hospitalizations for dehydration has steadily increased in recent decades. Specifically over the decade of 1990-2000 the rate of dehydration related hospitalizations in the US increased by 40.4% (64). Many studies reported high rates of hospitalizations for dehydration among the elderly population (37, 49). For example Warren et al (37) reported that the rate of hospitalizations per 10 000 elderly was 236.2 admissions with any listed diagnosis of dehydration and 49.7 admissions for dehydration as the principal diagnosis.

Additionally dehydration leads to the development of other diseases, which lead to hospitalizations and are directly related to an increase of healthcare costs. Indeed Zilberberg et al (63) found that hyponatremic patients have a higher co-morbidity index than patients with normal serum sodium. There is no doubt that these co-morbidities contribute to the need for emergency departments and an increase in length of stay (LOS) (59).

Although dehydration is a disease itself it is also appeared as comorbidity condition in a number of diseases. According to an AHRQ study of the 1997 Nationwide Inpatient Sample (NIS) (65) representing all patients in acute care hospitals, dehydration was diagnosed more commonly as comorbidity than as a principal diagnosis. Dehydration was the second most common comorbidity, occurring in 14% of all hospitalizations (64). Thus, dehydration may contribute to the increase of medical costs in an indirect way. It may be a marker of the severity of the underlying disease or it may add its own complications to those of the underlying disorder (63). For instance Chinnet al, performed a retrospective study of 435 patients admitted to a university hospital performing a multivariate analysis of these patients and found that the serum $[Na^+] < 135$ mmol/l was a significant and independent predictor ($p < 0.01$) of major complications in a patient's health status (66).

There is a wide range of studies in the literature analyzing and reporting the effect of dehydration as a comorbidity disease on the clinical and medical outcomes of different elderly patient such as orthopedic (61), with heart failure (60, 67, 68), pulmonary diseases (62, 69) and many others. For example Mukand et al, (61) and Zilberberg et al (62) in their studies found that dehydration prolongs length of stay for

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patients admitted with orthopedic and pneumonia respectively. Additionally Rabinovitz et al (69) found that hyponatremic patients had longer length of stay but also higher rate of hospital readmission.

In addition dehydration causes fluid deficits within cells which can affect the absorption of medications and averts drugs' expected effects. Therefore compromises optimal treatment of the underlying disorder (4) causing prolongation of treatment effects. Chronic disease and disorders, and multidrug therapy related to these conditions are common in elderly persons (70). Salmon (18) in his study pointed out that patients with dehydration have more difficulties in absorbing the medication for some diseases they face leading to a retardation of their healing.

Dehydration thus acts as an independent factor in the increase of the duration of hospitalization (27, 52, 58, 60–63, 66, 68, 69, 71); hospital readmission rate (58, 60), the need for intensive care (27, 58–60); use of medical support (52, 59) and the disposition to long or short term facility (27, 61). This is simply because dehydrated patients represent a sicker cohort among all those with the underlying disorder. These types of costs can be assumed as direct costs incurred by dehydration (Figure 1).

However there is no doubt that the indirect costs of hyponatremia such as time and productivity loss by patients and caregivers because of the illness as well as income lost by patients and family members, pose a substantial burden on households (Figure 1). However, as far as we know, no study has been conducted estimating these types of costs.

Overview of the methods for calculating costs

The studies found in the literature reflect the diversity of methods used to assess the economic burden from dehydration in the society. The methodological differences in the studies inherently prevent a formal meta-analysis from being performed. A discussion on the different methodologies used follows:

Firstly there is diversification among the studies in the definition of dehydration. Some studies define hospitalization for dehydration with the code ICD-9-CM or ICD-10-CM (International Classification of Diseases, Ninth Revision, Clinical Modification) as recorded in national database (2, 37, 49, 58, 60). For example Wakefield et al (2) in their study as a case they defined a patient with one of three ICD-9-CM codes as the principal diagnosis (i.e., reason for admission). The three principal diagnoses ICD-9-CM were hyperosmolality or hypernatremia, hypo-osmolality or hyponatremia; and volume depletion (22). While in other studies, where data are available authors define dehydration according to the serum sodium level of the hospitalized patients (27, 52, 59, 61–63, 67–69, 71) and even more they assessed the impact of different levels of dehydration on patients' outcome (52, 59, 67). For instance Turgutalp et al (59) looked on the severity of the disease. They separated their patients according to their

level of hyponatremia, depending on serum Na level; mild hyponatremia ($130 \text{ mmol/l} < \text{Na}^+ < 135 \text{ mmol/l}$), moderate hyponatremia ($120 \text{ mmol/l} < \text{Na}^+ < 130 \text{ mmol/l}$) and severe hyponatremia ($\text{Na}^+ < 120 \text{ mmol/l}$). However, most authors study only the economic effects of hyponatremia assuming that it is the most common type of dehydration (58, 60). Additionally there are some authors who used indices of dehydration such as BUN/Creatine ratio and systolic blood pressure (61).

Secondly the studies differ in the outcomes of measure. Some studies look only on hospital admission costs (37, 49) of dehydration while others look on hospital (27, 58–63, 67–69, 71) or (ICU) length of stay (LOS) (58, 60, 62), intensive care unit (ICU) costs of admission (58, 60), hospital readmission rates (58, 60), admission to ICU (59, 61–63), need of medical support (MV) (59, 62, 63) as well as disposition to short or long term care facilities (27, 61); all of which are drivers of costs.

Diversity in the definition of outcomes has also been observed. For example some studies look only on the cost of hospitalizations with a principal diagnosis of dehydration (37, 49). Data limitations prevent those studies to look on the cost of dehydration as a comorbidity condition. Hong (49) and Warren et al (37) conservatively estimate the economic burden associated with avoidable hospitalizations for dehydration by assuming equivalency between hospital charges and costs. Whereas authors, where data allow them, calculate total medical costs by summing the given standardized cost values for all hyponatremic patients found in inpatient facilities, outpatient facilities, professional services, and ambulatory services incurred in their study period (52).

Thirdly studies differ in their group of patients. A number of studies look on the impact of dehydration as a primary or secondary diagnosis of hospitalizations (27, 37, 49, 52, 58, 63, 71) while other studies look on its impact on a specific group of patients such as patients with heart failure (60, 67, 68), pulmonary diseases (62, 69) and orthopaedic (61).

Moreover studies differ in their setting of study. Although in many studies the sample of study was comprised from all the patients admitted in the hospital, some authors study a specific group of hospitalized patients (e.g. Emergency department, ICU etc). Turgutalp et al (59) for example estimated the clinical features, outcomes and costs of patients admitted to the emergency department (ED) and were identified with hyponatremia. While Mukand et al (61) looked only on patients who took surgery, therefore on surgical department.

It also worth mentioning that a number of studies look on only on patients admitted to a single centre (2, 27, 59, 61, 69) while other studies which mainly use data from databases with a sample of hospitals, multicentre (37, 49, 52, 58, 60, 62, 63, 67, 68, 71). A factor that directly affected their findings.

Finally the studies differ in their design and statistical analysis. Economic evaluations of dehydration have been done in different ways by different researchers; most of them performed retrospective studies using already collected longitudinal retrospective data of elderly patients hospitalized

in different academic and non-academic hospitals (2, 27, 37, 49, 52, 58–60, 62, 63, 67–69, 71). In contrast Mukand et al (61) performed a prospective, pilot study, where the subjects were patients who had surgery for orthopaedic reasons. Although the methodologies and hence the numerical results of these studies vary, all of them send a message for the proper management of the hydration status of patients, early detection and prevention so as to avoid an unnecessary increase in medical costs.

Review of the evidence on the economic burden of dehydration in elderly people

All of the studies reviewed assessed direct costs of dehydration disease, which include all the costs incurred by hospitalized patients. The numerical results of those studies vary because of the differences between the studies, mentioned above. In this section we present evidence on these direct costs.

Warren et al (37) found out that dehydration was 1 of 10 most frequent diagnoses reported for hospitalizations of persons over 65 and accounted for Medicare reimbursement to hospitals in excess of \$446 million for a single year. Zilberberg et al (63) estimated \$2289 to \$3480 rise in total hospital costs for each day for each patient hospitalized with hyponatremia. However, Shea et al (52) found that 1-yr mean inpatient costs for patients with hyponatremia were approximately \$10,636, more than 3 times higher than the previous estimate of Zilberberg et al (63). In their study, inpatient costs accounted for just over half of all direct medical costs.

In addition in their comparison of the hospital costs between hyponatremic and non-hyponatremic patients most of the authors found significant differences (58–60, 62, 63, 71). For example Callahan et al (71) found that patients with hyponatremia cost 14266\$ per admission compared to the non-hyponatremic patients which cost 13066\$. Similarly Zilberberg et al (63) found almost 3000\$ difference between the two groups.

Furthermore, increases in length of stay (LOS) due to the negative effects of hyponatremia on the health of patients have been shown by a number of authors (27, 52, 58, 60–63, 66, 68, 69, 71). The difference in hospital LOS at first admission between HN and non-HN patients in the study Amin et al (58) was 1.1 days. Similar to that reported in a study conducted by Shorr et al (67) which found a 0.7 and 1.28 day greater LOS for HN and severe HN HF patients, respectively, in comparison with non hyponatremic HF patients]. Zilberberg (63) and Callahan et al (71) performing retrospective cohort analyses and making the same comparison reported a difference of 1.4 days and 2.0 days respectively.

Patients diagnosed with hyponatremia are significantly more likely to be readmitted to hospital for any cause than patients with similar demographics and characteristics who do not have hyponatremia (58, 60). Hospital readmissions are a significant contributor to total healthcare costs, with some being entirely avoidable with increased standards of care. Gheorgheade et al (68) in their studies which were conducted on clinical trial

patients with acute heart failure found that HN patients in comparison to non-HN patients reported a significant increase in readmission rates. However, Amin et al (60) reported that hyponatremia was associated with an incremental increase ranging between 14% and 17% for hospital readmission for any cause.

Zilberberg (63) and Callahan et al (71) reported that HN patients had a significantly greater need for ICU (4%–10%). Hyponatremia is a very relevant electrolyte disorder among people who report to the emergency department (ED). Focusing on ICU population Zilberberg et al (63) found out that hyponatremia was twice as frequent as in the overall hospital population (11.3%) and its independent association to worsened outcomes persisted. For example, hyponatremic ICU patients were significantly more likely to experience such dire clinical outcome as hospital death, as well as to require mechanical ventilation. With an average adjusted cost of MV of \$1,500 per day, this increased utilization is likely to add substantially to the overall costs of care. Similarly Turgutalp et al (59) in their study reported positive relationship between the age and the need for intensive care and ventilator support. Amin et al (58) in their study estimated ICU costs per admission and found that hyponatremic patients costs approximately 1600\$ more than non-hyponatremic patients.

Severity of hyponatremia prognosticates adverse outcomes, especially when hyponatremia develops in hospital. According to Wald et al (27) patients with hospital acquired hyponatremia have higher risk of death compared to the community acquired hyponatremia. Moreover patients with hospital acquired hyponatremia were shown to be frequently associated with delays in the initiation of treatment.

At aggregate level, the potential national saving from avoidable hospitalizations in elderly patients (older than 65) hospitalized for dehydration has been estimated in \$1,14 billion for 1999 (49).

Final considerations

This literature review has presented the available evidence on the economic burden related to dehydration. However before concluding its most important results, some of the methodological issues in many of the studies that were included will be highlighted. First, in most retrospective cohort studies the prevalence of hyponatremia illness was based in large part on the number of hospitalizations with the code ICD-9-CM or ICD-10-CM as recorded in a national database (49, 58, 60, 62, 63, 72). There was evidence that these codes for hyponatremia represent only a low proportion of the patients admitted to the hospital and were experiencing hyponatremia, due to the low sensitivity of the diagnosis code (73). Moreover, a high proportion of hyponatremia in the hospital setting is iatrogenic and hospitals may be reluctant to include the code in the discharge data. Any retrospective analysis may have thus faced the same study limitations (73).

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Second, the studies which used individual comorbidity indexes mainly used administrative codes. This is relatively crude and does not account for the severity of the condition in question. Therefore the inability to incorporate the severity of the comorbidities might have led to some unmeasured confounding in the analysis. The substantial variations in study designs and definitions described earlier also make comparisons tricky and meta-analysis infeasible. There is considerable heterogeneity in methodologies used in the papers.

Taking into consideration the methodological issues highlighted here we can still conclude that dehydration already imposes substantial financial costs in the society. According to the degree or magnitude of the dehydration in hospitalized patients increase costs by 7% to 8.5%. Higher cost will be associated with an increase in hospital mortality, as well as with an increase in the utilization of ICU, short and long term care facilities, readmission rates and hospital resources, especially among those with moderate to severe hyponatremia. The more severe the level of hyponatremia, the more likely a patient's hospitalization will be prolonged (27, 71). Data available from both the US (74) and Europe (75) show that mortality and medical costs are reduced by effective treatment of hyponatremia (58, 60, 62, 63, 67, 68). However, most of the research is only based on direct costs of dehydration. Therefore future research needs to be done in estimating indirect costs associated with it in order to have a more complete picture of its economic burden.

Dehydration as a syndrome cannot be treated merely by throwing water at it! Surveys should look not at its mere sentinel presence, but whether it was addressed in a multi-faceted method that accounts for underlying cause(s), considers pharmacology involved, reviews the involvement of the physician and staff, addresses moral principles that arise, and places it in the context of individual circumstances. We need a better reality in long term care that addresses education regarding modern thoughts about dehydration, the importance of careful clinical approaches, the concept of unavoidability, and the need to reconsider how we survey this complex entity. Patients' admission and discharge statistics should accurately include the diagnosis of dehydration as a comorbidity or main disease, in order to help to patient management and to allow appropriate research and comparisons across centres.

Rapid recognition and optimal treatment of depressed serum sodium or osmolality can reduce the risk of death and symptom severity, permit less intensive care, reduce the duration of hospitalization and associated costs, increase success in treatment of underlying comorbid conditions, and improve quality of life. This implies a healthier and automatically more productive population. In their studies Licata (76) and Leadbetter et al (77) have shown that treatment of hyponatremia and dehydration reduces the frequency and severity of many side effects. These benefits relieve patients from mental and economic costs, increasing their quality of life.

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