Int J Biometeorol (2015) 59:249–263
DOI 10.1007/s00484-014-0861-1

REVIEW PAPER

Association with meteo-climatological factors and daily emergency visits for renal colic and urinary calculi in Cuneo, Italy. A retrospective observational study, 2007–2010

Vincenzo Condemi · Massimo Gestro · Elena Dozio · Bruno Tartaglino · Massimiliano Marco Corsi Romanelli · Umberto Solimene · Roberto Meco

Received: 15 April 2014 / Revised: 9 June 2014 / Accepted: 13 June 2014 / Published online: 27 June 2014

Abstract The incidence of nephrolithiasis is rising worldwide, especially in women and with increasing age. Incidence and prevalence of kidney stones are affected by genetic, nutritional, and environmental factors. The aim of this study is to investigate the link between various meteorological factors (independent variables) and the daily number of visits to the Emergency Department (ED of the S. Croce and Carle Hospital of Cuneo for renal colic (RC) and urinary stones (UC) as the dependent variable over the years 2007–2010.

The Poisson generalized regression models (PGAMs) have been used in different progressive ways. The results of PGAMs (stage 1) adjusted for seasonal and calendar factors confirmed a significant correlation ($p<0.03$) with the thermal parameter. Evaluation of the dose–response effect [PGAMs combined with distributed lags nonlinear models (DLNMs)—stage 2], expressed in terms of relative risk (RR) and cumulative relative risk (RRC), indicated a relative significant effect up to 15 lag days of lag (RR>1), with a first peak after 5 days (lag ranges 0–1, 0–3, and 0–5) and a second weak peak observed along the 5–15 lag range days. The estimated RR for females was significant, mainly in the second and fourth age group considered (19–44 and >65 years): RR for total ED visits 1.27, confidence interval (CI) 1.11–1.46 (lag 0–5 days); RR 1.42, CI 1.01–2.01 (lag 0–10 days); and RR 1.35, CI 1.09–1.68 (lag 0–15 days). The research also indicated a moderate involvement of the thermal factor in the onset of RC caused by UC, exclusively in the female sex. Further studies will be necessary to confirm these results.

Keywords Biometeorology · Temperature · Renal colic · Urinary calculi · Emergency department visits · Preventive medicine

Introduction

Recent reports indicated that meteo-climatogical factors may play an important role both in the onset of acute pathologies as well as in the reactutization of chronic diseases, mainly at respiratory and cardiovascular level. The association between meteorological factors and the variability of daily and weekly number of patients visits to Emergency Department (ED) has been the topic of previous studies performed in different countries (Makle et al. 2001; Rusticucci and Bettolli 2002). Great attention has also been given to study the impact of heat waves on mortality and morbility both on local and national

V. Condemi
Department of Biomedical Science for Health, Centre for Research in Medical Bioclimatology, Thermal and Complementary Medicine and Wellness Sciences, Università degli Studi di Milano, Milan, Italy

M. Gestro · U. Solimene (✉)
Centre for Research in Medical Bioclimatology, Thermal and Complementary Medicine and Wellness Sciences, Università degli Studi di Milano, Via Cicognara 7, 20129 Milan, Italy
e-mail: umberto.solimene@unimi.it

B. Tartaglino
S. Croce and Carle Hospital of Cuneo, Cuneo, Italy

E. Dozio · M. M. Corsi Romanelli
Department of Biomedical Science for Health, Università degli Studi di Milano, Milan, Italy

M. M. Corsi Romanelli
Service of Laboratory Medicine 1, Clinical Pathology, Department of Health Services of Diagnosis and Treatment-Laboratory Medicine, I.R.C.C.S. Policlinico San Donato, San Donato Milanese, Milan, Italy

R. Meco
Università Cattolica di Milano, Milan, Italy

scales (Kovats et al. 2004; Besancenot 2002), also considering specific city-population subgroups (Stafoggia et al. 2006) and exploring city-specific factors that might explain variations in the association between temperature and mortality across cities (Curriero et al. 2002). A recent multicenter study (Michelozzi et al. 2009) demonstrated a significant association between heat waves and respiratory visits to ED, whereas no association has been observed with cardiovascular and cerebrovascular ED visits.

A global analysis of the literature in the field of climate changes, health, and mortality indicated that most of the studies have focused on individual cities (Thirion 1992; Semenza et al. 1996; Ballester et al. 1997; Dessai 2002, 2003; Nastos and Matzarakis 2006; Revich and Shaposhnilkov 2008; Hu et al. 2008), and only few studies considered wide geographic areas such as a study on winter mortality in England and Wales (Johnson and Griffiths 2003). A recent meta-analysis of current literature about the effects of temperature fluctuations (summer and winter) upon mortality among the elderly (Yu et al. 2012) indicated that both hot and cold temperatures increased mortality, but the magnitude of heat-related effects appeared to be greater.

The prevalence of urinary stones (UC) is increasing in Western countries, and it has been closely linked to race, diet, geographical, and climatic factors (Association of Italian Urologists 2007). In industrialized countries, the prevalence of UC has been estimated between 4 and 20 %, with an annual incidence of hospitalizations variable from 0.04 to 0.30 % and a ratio between male and female of 2:1. The prevalence of nephrolithiasis UC in Italy has been estimated between 6 and 9 %, with about 100,000 new cases/year (Borghi et al. 1990). An increased incidence of UC has been observed in areas with hot temperature throughout the year or during summer. This has been linked to a decreased urine volume, secondary to an increase in skin transpiration, increased urinary osmolarity, increased concentration of calcium and oxalic acid and decrease urinary pH (Robertson et al. 1975). The hypothesis of an association between weather and climate variables in the onset of UC has been advanced in several scientific works published both in the last decade as well as previously (Fujita 1987). Some of these papers also explored the risk of UC in workers exposed to specific geo-working conditions, such as American troops in a desert area and men working in steel industry at hot temperatures (Pierce et al. 1945; Soucie et al. 1996; Altan et al. 2005; Evans and Costabile 2005).

The importance of the thermal factor in the etiopathogenesis of the UC has also been confirmed by studies performed in Arabia (Al-Hadramy 1997) and Taiwan (Chen et al. 2008). In contrast, a work carried out in the City of Mumbai indicated that the disease is unrelated to season, but it is also true that in this geographic area temperature do not significantly vary between summer and winter (Hussain et al. 1990).

Two recent papers also explored the association between renal colic (RC) and climatic conditions, in particular temperature and solar radiation, in two Italian cities, Padua (Boscolo-Berto et al. 2008) and Parma (Cervellin et al. 2011). Both studies reported a significant association between temperature and RC. It is important to note that the geographical areas evaluated in the two studies are both located within the Pianura Padana (Po Valley) at the outline of a topographic amphitheater, Alpine Mountains to the northwest and Apennine Mountains to South. Specifically, Padua has a height of 12 m above sea level with an average height of the province of 16 m, and Parma is 57 m high with an average of its province of 288 m. These areas should be considered comparable for their meteo-climatogical factors with the City of Cuneo and its province. Another study (Cervellin et al. 2012) suggests that the hot and dry climate would play a role accelerating the process of stone formation. A critical review of the medical literature relating RC and UC to ambient temperature strongly indicated that heat does play a role in the pathogenesis (Fakheri and Goldfarb 2011). The real mechanisms linking whether UC and RC are now not well understood. Particularly striking has been the hypothesis advanced some years ago of a possible link between increased CO_2 in the atmosphere (now close to 400 ppm) and increased prevalence of RC (Curtin and Sampson 1989). Although the mechanisms have not yet been identified, this hypothesis remains of interest.

An increased risk of UC incidence in the USA has been suggested by an innovative approach using a prediction model grafted on temperature trends (Brikowsky et al. 2008). This model predicted a nationwide increase in the prevalence of UC of about 10 and a 25 % increase in the annual cost of ED visits by 2050. This scenario is in line with what has been estimated by the IPCC (IPCC4 2007).

In the present work, our aim was to test the hypothesis that different urological disorders may be etiologically influenced and/or determined by temperature trends in association to other meteo-climatogical factors in a specific geographic area, the Province of Cuneo (Italy), that for its territorial peculiarities is suitable to be compared to the Provinces of Padua and Parma previously studied (Boscolo-Berto et al. 2008; Cervellin et al. 2011).

ED database

The present study is a retrospective observational study based on the ED visits database (DB) of the S. Croce and Carle Hospital of Cuneo over the years 2006–2010, for a total of 1,820 days. Data are described in anonymous form according to privacy rule. They include: a numeric code for each medical record; a progressive number for patient visited at ED; age; gender; year, day, hour, and minute of access; municipality of residence; mode of hospital discharge (sent back home, refused admission, removal, and hospitalized). The symptoms reported by the patients and the triage code of access (white, green, yellow, and red) are reported in specific fields of clinical interest. A first field contains the diagnosis and the corresponding ICD-9 code, described as DIA-1, and the sequence of five additional fields (from DIA-2 to DIA-6), where subsequent ICD-9 reclassification, whether made, are indicated.

Other clinical data available for each patient are: maximum and minimum pressure, respiratory rate, fraction of inspired oxygen, tympanic temperature, and oximetry. Lastly, the DB is accompanied by two additional fields, filled as text, containing the physical examination and the medical history profile of the patient.

Meteorological and climatological databases

We used two specific climatological DB:

(a) DB containing the climatological time series of Cuneo and its province (Collana di Studi Climatologici in Piemonte 1998). These data contain the thermometric time series from 1951 to 1986 and the rainfall observations from 1913 to 1986; and
(b) The climatological DB of the Province of Cuneo, over the years 2006–2010, released online by the Meteorological Data Bank ARPA Piemonte (http://www.arpa.piemonte.it/) with daily data in Excel format.

The monitoring stations chosen are Cuneo (two stations), at the height of 530 m, Bra, 44°42′0″N 7°51′0″E, at the height of 290 m, Alba Tanaro, 44°43′0″N 8°5′0″E, with an altitude of 170 m, Mondovi, 44°23′0″N 7°49′0″E, located at 395 m, Fossano, 44°33′0″N 7°44′0″, situated at a height of 375 m, Boves, 44°20′0″N 7°33′0″E, with an altitude of 560 m and Costigliole Saluzzo, 44°34′0″N 7°29′0″E, with an altitude of 460 m. The DB contains meteorological data calculated as average daily temperature (T_{max}, T_{mean}, and T_{min}), hygrometer observation (RH_{max}, RH_{mean}, and RH_{min}), wind observation (W_{max}, W_{mean}, and W_{min}) expressed as average speed in meter per second, maximum gust in meter per second, wind calm duration in minutes, and barometric pressure (P_{max}, P_{mean}, and P_{min}). The DB also contain rainfall (in millimeter) and snowfall (in centimeter) observations and the accumulation of snow on the ground. A specific field shows the pyranometric data with daily average values of total radiation (TR_{mean}) espressed in megajoule per square meter.

The geographic area studied borders at west with the southeastern France (Departments of Hautes-Alpes, Alpes de Haute Provence, and Alpes Maritimes in the region Provence-Alpes-Côte d'Azur), north with the Province of Turin, east with the Province of Asti, and south with Liguria—Provinces of Imperia and Savona). It has an area of 6,903 km^2, and it is the third largest province in Italy. According to data updated on December 31, 2010, the number of residents is 592,303 units, with a density of 63 habitants/km^2. There are 250 municipalities with an average altitude, detected at the site of each municipal of 558,112 m, which is higher than the average altimetry of Italy of 337 m. The habitants of Cuneo are 55,714, including 64,356 habitants living in the nine municipalities bordering with the city. The total number reaches the 120,070 units. From a climatic point of view, the Province of Cuneo, characterized by hilly areas and high plains, according to the classification system developed by W. Koeppen, is placed in the mesothermal C band (temperate climate of mid-latitude).

Methodology used and inclusion/exclusion criteria

The total number of ED visits is 304,040 with a mean of daily hospitalizations of 208 and an average age of 42.30 years. We extracted the codes ICD-9 7,880 and 5,929 for a total of 4,834 cases.

Due to the complexity of the DB and the presence of several diagnostic data in the fields next to DIA-1, we introduced specific inclusion and exclusion criteria to identify the cases to be included in the study.

Inclusion criteria are:

(a) Code ICD-9 7880 (DIA-1—first diagnosis) relative to RC, with full inclusion in the study;
(b) Code ICD-9 7880 (DIA-2—second diagnosis), confirmed by medical history and physical examination, with the presence of symptoms or clinically related diseases in DIA-1;
(c) Code ICD-9 7880 in DIA-2, with the presence in DIA-1 of symptoms or diseases clinically unrelated to ED visits and especially without mention of significant pathology in other diagnosis;
(d) Code ICD-9 5929 relative to UC (DIA-1—first diagnosis) with symptoms, in the field of medical history and physical examination, of signs clinically related to urinary obstruction, without mention of significant pathology in other diagnosis; and
(e) Code ICD-9 5929 in DIA-2, with symptoms or disease entities in DIA-1 correlated with urinary obstruction, further confirmed by symptoms (in medical history) and signs (in examination).

In order to confirm the clinical observations the following symptoms, signs, and clinically related diseases have also been considered but not included in the inclusion criteria: hydronephrosis (ICD-9 591), colic or pain in the lumbar or abdominal quadrants (ICD-9 78900, 78901, 78903, 78904, 78906, 78907, 78909, and 7242), urological symptoms and signs (ICD-9 5997), hematuria and increased urinary frequency (ICD-9 78841), retention (ICD-9 78820), urinary tract infection (ICD-9 5990 and 5550), and other signs or symptoms such as fever (ICD-9 7806) and vomiting (ICD-9 7870 and 78701).

Exclusion criteria are:

(a) The year 2006 has been excluded from the search for reasons of comparability with other information present only in the subsequent years (physical examination and medical history). For this reason, the research was carried out from 2007 to 2010.
(b) All cases with a medical history of lithotripsy (ESWL) were excluded because ESWL may be a potential confounding factor for the analysis.
(c) Patients with a second admittance to ED within the 15 days from the first.
(d) Patients with symptomatic tumors of the urinary tract, etiologically important in the onset of acute urinary obstruction.
(e) Code ICD-9 7880 in DIA-2 with symptoms or diseases present in DIA-1 not related to the clinical group in question or of greater importance and clearly at the origin of the ED visits (cross of data of diagnosis, medical history, and examination).
(f) Code ICD-0 5929 in DIA-1, with symptoms or diseases in DIA-2 not related to the clinical group in question or of greater importance and clearly at the origin of the ED visits in the absence of symptoms (in medical history) and signs (in examination) clinically related to urinary obstruction.
(g) Nonresidents and all patients whose municipality of residence does not appear in the corresponding field.
(h) People living in municipalities with an altitude>1,000 m for obvious differences with the mean climatic characteristics of the geographical context analyzed.

Statistical methods

Climate data were analyzed using established systems of climatology descriptive statistics. It has been stratified by T_{mean}, RH_{mean}, P_{mean}, and TR_{mean}. In particular, the thermometric values were stratified by replicating the models used in a previous work (Cervellin et al. 2011) with seven thermometric classes: <0, 0–5, >5≤10, >10≤15, >15≤20, >20≤25, and >26–30 °C. Central to improve the control of the geographic variability, the climatological database 2007–2010 was used a thermometric reference time series (RTS) to test a candidate station (CS). The station chosen as a CS is Cuneo Cascina Vecchia. The reference series was constructed on the basis of the geo-topographic characteristics of the monitoring stations (see previous Meteorological and Climatological Databases), with some minimum criteria for inclusion and exclusion: in particular, a minimum distance between CS and other stations of 200 km and an altimetry variation of 400 m (Peterson and Easterling 1994) using the correlation coefficient of Bravais–Pearson. Then we carried estimates of associative measures between the different climate covariates and the number of daily ED visits for RC and UC using the correlation coefficient of Bravais–Pearson. In the overall design, this last methodology was considered exploratory.

Inferential statistical analysis has been performed in two progressive model stages. The response variable is the number of daily ED visits and its subgroup counts: females, males and sex-specific age. Several different covariates were included in the models: all the climate covariates, namely, T_{mean}, RH_{mean}, P_{mean}, and TR_{mean}, gender, age (in four classes: 0–18, 19–44, 45–65, and >65), days of week (dow—1 Monday…7 Sunday), weekends, and summer holidays with three categories: 1=from July 15 to 31 and August 16 to 31, 2=from August 1 to 15, and 0=all other days. We have also included years, seasons, and months to control seasonal variations and trend.

Stage 1

The first stage was divided into two consequential procedures, based on the construction of a simple Poisson generalized regression model (PGAM) applied to the time series, aimed to estimate, preliminarily, the association of several meteorological covariates and the daily number ED visits. This was run in a backward mode with all the climate covariates included and response variable, the number of daily accesses to ED visits. The wind field has been excluded for consistent unhomogeneous values in the comparison between the different stations. A natural cubic spline to control seasonal variations was included (time 7^*4), days of week (dow), and summer holidays as factors. Finally, the Akaike Information Criterion (AIC) was used to find the best fit model.

Stage 2

Many studies, especially in the last decade have reported a delayed effect of temperature on various diseases and mortality (Schwartz 2000; Goggins et al. 2012; Guo et al. 2012; Bhaskaran et al. 2013). Taking into account the existence of latent periods for RC based on the concept of dose–response at different times, estimated in the monthly order with silent symptoms before the onset of the disease (Evans and Costabile 2005), it has been programmed as a new statistical procedure. We used a PGAM model in combination with distributed lags nonlinear models (DLNMs) family and the libraries R statistics mgcv, dlnm, and splines to estimate the lagged effects and their distribution over the time (Gasparrini

2011). We assume that the effect of temperature is linear while modeling the relationship through a natural cubic spline with 5 degrees of freedom (*df*) and internal knots placed at equally spaced quantiles, centered at −1.5 °C (mean into minimum and 25th), with a 4 degrees polynomial function, by lags 1. To correct the effects for seasonality and long-time trend, we have included a smooth function with 7 degrees of freedom/year, associating the variable dow as factor. The DLNM methodological framework has been divided into ten progressive lag steps: lag ranges 0–1 days (step 1), 0–3 days (step 2), 0–5 (step 3), … 0–10, 0–15, 0–20, 0–30, 0–40, 0–50, and 0–60, assuming 5 °C increase in T_{mean} (baseline) and using a certain degree of overdispersion (quasi-Poisson). The same analysis was performed in subsequent subgroup analysis for sex-specific and age-specific layer, in the light of the results of the previous stage (stage 2) of the modeling. Estimation of the relative risk (RR; 95 % CI) was the final outcome of the DLNM modeling together with the graphical representation of the cumulative relative risk (RRC).

Stage 3

We carried a bidimensional DLNM representation through a natural and nonnatural spline. The DLNM statistical analysis was repeated for subgroups of the resident population visits to the ED: (a) specific analysis for Cuneo City and neighboring towns and (b) all other municipalities. Finally, to confirm the previous outputs modeling, we performed a sensitivity analysis (stage 4) with the following characteristics: modeling for daily number ED and daily number ED sex-specific splines, with 5 *df* for temperature and knots placed at equally spaced value, centered at −1.5 °C.

There were variations in temperature increase of 3, 4, 6, and 7 °C (baseline 5 °C), natural spline with 6, 8 and 9 *df*/year (baseline 7*4/year), and lag ranges of 0–3 and 0–5.

The statistical analyses were performed using R Statistical software version 3.0.1.

Results

Analysis of temperature and precipitation from time series (series from 1951 to 1986) related to climate data of Cuneo showed a T_{mean}<+18 °C with a T_{mean}>−3 °C in the middle of the winter season. According to W. Koppen climate classification, the Cuneo City is classified as CF, but with the possibility to be included both in the subgroups CFb and CFa. In fact, according to climatological data set, the city may be classified as CFb (with T_{mean}<22 °C in the hottest month. On the contrary, the results of the analysis performed only on the last 5 years suggested the existence of a transition regime with the prevalence of the type CFa characterized by an average temperature>22 °C in the hottest month. This results is consistent with some thermometric time series consulted on a global scale (GissTemp: http://data.giss.nasa.gov/gistemp/ and HadCRU: http://www.metoffice.gov.uk/hadobs/hadcrut4/).

The rainfall pattern has two peaks, one in spring with a maximum in May and one in autumn with a maximum in October, and two minima, one during the winter in January and one during the summer in July or August. During winter, the snowfalls are the most abundant among all the chief towns of Italy. Tables 1 and 2 summarize the climate data for the period 2006–2010 together with the ED data. The calculated geodetic distances of Cuneo to the other weather stations are: Alba 51.8 km, Bra 41.8 km, Mondovì 21.9 km, Fossano 22.3 km, and Costigliole Saluzzo 19.0 km. It was also included the station of Boves located in the urban belt of Cuneo (<7 km). Stations are located at an altitude ranging from 170 to 560 m. The correlation coefficient calculated between thermometric reference time series (RTS) and the candidate station (CS) was r≥0.98 (T_{mean}), r>0.91 (T_{max}), and r>0.90 (T_{min}), suggesting an overall consistent homogeneity between the compared series (Table 3). The same was observed for TR_{mean} and $RH_{mean.}$ The missing values of the total observations were <0.03 % for all weather stations.

The number of ED visits was 72,373 (2006), 71,689 (2007), 76,645 (2008), 78,009 (2009), and 77,697 (2010), for a total of 376,413 episodes. There was a partial increase in the number of ED visits after the 2006, likely as a result of an economic rationalization processes of the Italian health system, with a consolidated data in the range 76,645–78,009 for the period 2009–2010.

For the aim of our research, we selected the codes ICD-9 7880 (RC) and 5929 (UC). The database did not contain specific information on the composition of RC and on the presence of hyperparathyroidism. No specific information on the hypercalcemic state of the patients was identified in the medical history field. By applying the inclusion/exclusion criteria, the number of RC cases was reduced from 4,834 to 4,051. Cases excluded were for readmissions, nonresident patients and residents in area with an altitude>1,000 m.

This is a summary of the number of accesses/year: 986 (2007), 1,028 (2008), 1,030 (2009), and 1,007 (2010). There were 2,270 males (56.04 %) and 1,781 females (43.96 %). The average number of daily accesses was 2.77, with a peak in July (3.23) and a minimum in December (2.23). The daily number of ED visits specific for sex and age are: female age 1–18 (105), 19–44 (1,087), 45–65 (416), and >65 (173). Male age: 1–18 (28), 19–44 (935), 45–65 (1,041), and >65 (266).

According to code classification, cases were distributed as follow: 3,867 (ICD-9 7880), 87 (ICD-9 5929), 20 (ICD-9 5990—urinary tract infection), 19 (ICD-9 591—hydronephrosis), and 7 (ICD-9 5950—acute cystitis).

Table 1 Statistical summary of climatological variables, all ED visits, sex, and specific age

Variables	Units	Mean	SD	Min	25th	50th	75th	Max
T_{mean} (°C)	1,461	12.085	8.1520	−7	5.0	12.0	19.2	27
T_{max} (°C)	1,461	17.941	8.9019	−3	10.6	18.1	25.8	34.7
T_{min} (°C)	1,461	7.122	7.4812	−11	0.6	7.4	13.5	21.8
RTS_{mean} (°C)	1,461	12.081	8.1834	−8	1,006.0	1,011.0	1,015.0	27.1
RTS_{max} (°C)	1,461	17.931	8.9809	−3	7.0	13.0	20.0	35
RTS_{min} (°C)	1,461	7.072	7.4928	−12	58.0	68.0	78.0	21.7
Bar (hP)	1,461	1,010.36	7.124	978	1.0	1.0	2.0	1,031
TR (MJ/m^2)	1,461	13.496	7.9494	1	0.0	1.0	2.0	30
RH (%)	1,461	67.81	15.230	27	0.0	0.0	0.0	100
ED visits	1,461	2.77	1.739	0	0.0	1.0	2.0	10
Sex males	1,461	1.55	1.271	0	0.0	1.0	1.5	8
Sex females	1,461	1.22	1.144	0	0.0	0.0	1.0	8
Age 1	1,461	0.09	0.308	0	0.00	0.00	0.00	1
Age 2	1,461	1.38	1.231	0	0.00	1.00	2.00	5
Age 3	1,461	1.00	0.999	0	0.00	1.00	1.50	5
Age 4	1,461	0.30	0.561	0	0.00	0.00	1.00	3

Clinical information included in the following fields (from DIA-2 to DIA-6) were analyzed on the basis of the inclusion/exclusion criteria previously proposed and further revised on the light of the information available in the medical history and in the physical examinations sections: we found 58 cases which refused any treatment.

In agreement with data reported in previous papers, the mean age±SD of all patients included in our analysis was 44.46±15.73 years, with a median of 43. After classification according to gender, the mean age was 47.80±14.10 years, with a median of 47 for male and 40.20±16.66 years, with a median of 47.80 for female. After patient classification by age, we observed 133 cases in the group 0–18 years, but none of these aged ≤5 years, according to previous observation.

Residents of Cuneo and surrounding municipalities (2,634 cases, 65.02 %) were then analyzed separately from other municipalities (1,417 cases, 34.98 %). The triage codes assigned at the admittance were in line with data previously reported: 0.52 % of patients had a white code, 46.33 % had a green code, 53.15 % had a yellow code, and none had a red code.

We also evaluated the incidence of RC in pregnant patients due to its importance in the clinical differential diagnosis and in the evaluation of diagnostic and therapeutic intervention risks for both mother and fetus at the emergency. The numbers of pregnant women visits to ED for RC were: 22 in 2007, 38 in 2008, 29 in 2009, and 30 in 2010. Compared to the total number of ED visits for RC, pregnant women represented the 1.89 % (22/1,164) in 2007, 3.09 % (38/1,229) in 2008, 2.36 % (28/1,186) in 2009, and 2.56 % (30/1,174) in 2010. The percentages of hospital admission after ED visits were: 27 % in 2007, 26 % in 2008, 28 % in 2009, and 46 % in 2010.

Table 2 Monthly climatological variables and ED data—max, min, and means—Cuneo 2007–2010

Months	T_{mean}	T_{max}	T_{min}	SRT_{mean}	ED visits count	ED visits mean
Jan	1.51	7.08	−8.90	1.40	305.00	2.46
Feb	3.69	9.79	−9.50	3.63	297.00	2.63
Mar	7.86	13.97	−4.40	7.84	354.00	2.85
Apr	12.35	18.15	1.30	12.37	320.00	2.67
May	16.81	22.70	5.00	16.84	357.00	2.88
Jun	20.40	26.59	9.90	20.44	383.00	3.19
Jul	23.24	29.98	10.10	23.25	400.00	3.23
Aug	21.91	28.35	8.10	21.95	354.00	2.85
Sept	17.21	23.33	4.60	17.25	329.00	2.74
Oct	12.02	17.45	−1.20	12.04	339.00	2.73
Nov	6.37	10.97	−5.10	6.40	337.00	2.81
Dec	1.17	6.47	−11.30	1.08	276.00	2.23

Table 3 Matrix of Pearson correlation coefficients between weather variables, candidate station (Cuneo Cascina Vecchia), and reference time series

Variables	T_{mean}	T_{max}	T_{min}	RTS_{mean}	RTS_{max}	RTS_{min}
T_{mean} [a]	1	0.976	0.974	0.994	0.978	0.97
T_{max} [a]		1	0.911	0.974	0.991	0.904
T_{min} [a]			1	0.976	0.913	0.983
RTS_{mean} [b]				1	0.976	0.972
RTS_{max} [b]					1	0.907
RTS_{min} [b]						1

[a] Candidate station (Cuneo)

[b] Reference time series (other stations)

Table 4 (Stage 1) Poisson model with climatological factors adjusted for seasonal and calendar factors (long[a] and short time) before backward procedure

Variables	Estimate	$Pr(>\|z\|)$
Intercept	1.9723062	0.4507
T_{mean}	0.0155772	0.0268*
RH_{mean}	0.0002371	0.8707
$Press_{mean}$	−0.0010628	0.6786
TR_{mean}	0.0006702	0.8700
Holidays	0.0027293	0.9608
Dow 2	−0.2094640	0.000387***
Dow 3	−0.0955361	0.095130#
Dow 4	−0.1624343	0.005278**
Dow 5	−0.1449957	0.012326*
Dow 6	−0.0663206	0.243493##
Dow 7	−0.0667488	0.241136

Significant codes: *** 0, ** 0.001, * 0.01, # 0.05, and ## 0.1

[a] ns (time 7* 4)

For information purposes only, the number of RC patients affected by diabetes has also been investigated. Diabetes was diagnosed in 44 RC men and 15 RC women. Patients were also evaluated for hypertension. A total of 293 RC cases were also hypertensive. According to the established inclusion/exclusion criteria, 32 cases falling in ESWL and one with kidney cancer were excluded.

In few cases, we also considered some risk factors such as urological surgery for left pelvic ureteral stenosis due to periureteral scar tissue, abnormalities of the ureteropelvic junction, and also some hospitalization for gout, hypercalcemia, hyperparathyroidism, surgery for stenosis of the right pielo-ureteral junction, plastic of the left pielo-ureteral junction, and history of sarcoidosis with axillary lymphadenopathy. Unfortunately, due to the low number of patients with the previously described pathologies, we were not able to reach a conclusion worth mentioning.

The Pearson correlation analyses, merely exploratory and made on a monthly basis, showed the following coefficients: r=0.60 for T_{mean} and ED visits r=0.56 for TR_{mean} and P_{mean}. The correlation coefficient between T_{mean} and TR_{mean} was very high (r=0.82), suggesting a possible problem of collinearity. The correlation coefficient between RH_{mean} and ED visits was slightly negative (r=−0.11), in agreement with data reported in previous papers. In particular, cross-data analysis between thermometric classes of T_{mean} and cases observed in ED (frequency percentages of the corresponding episodes of RC and UC) has confirmed a trend shown in previous studies (Cervellin et al. 2011).

We then constructed a statistical model of the PGAMs family (statistical stage 1) in the backward mode, adjusted for time and calendar factors, first including all the meteorological covariates and then eliminating those with low significance. We observed an association of the thermal component (p<0.03), whereas no significance was observed for the other four parameters (TR_{mean}, RH_{mean}, P_{mean}, *and* TR_{mean}, *with a p* value or>0.05 for all (Table 4). The second model (PGAMs combined with DLNM—statistical stage 2), whose outcome is expressed in terms of RR (95 % CI) and graphically represented by RR and CRR for each lag range, showed the following results: model all count ED visits: step 1 (lag time 0–1), RR 1.11, CI 1.03–1.19; step 2 (lag time 0–3), RR 1.14, CI 1.05–1.23; step 3 (lag time 0–5), RR 1.14, CI 1.05–1.25; step 4 (lag time 0–10), RR 1,22, CI 0.97–1.54; and step 5 (lag time 0–15), RR 1.20, CI 1.04–1.38. The last step of the modeling considered three steps (lags 0–5, 0–10, and 0–15) specific for sex and age, excluding the age group 0–18

Table 5 Results DLNM—RR with a 5 °C unit increase in T_{mean} for ED visits (ten steps) for females and males (five steps)

Lag steps	Lag ranges (days)	RR	95 % CI low	95 % CI high
Step 1	0–1	1.11	1.03	1.19*
Step 2	0–3	1.14	1.05	1.23*
Step 3	0–5	1.14	1.05	1.25*
Step 4	0–10	1.22	0.97	1.54
Step 5	0–15	1.20	1.04	1.38*
Step 6	0–20	1.14	0.96	1.36
Step 7	0–30	0.98	0.75	1.27
Step 8	0–40	0.79	0.55	1.14
Step 9	0–50	0.90	0.56	1.44
Step 10	0–60	1.09	0.59	2.00
Step 1 females	0–1	1.17	1.06	1.31*
Step 2 females	0–3	1.22	1.08	1.38*
Step 3 females	0–5	1.27	1.11	1.46*
Step 4 females	0–10	1.42	1.01	2.01*
Step 5 females	0–15	1.35	1.09	1.68*
Step 1 males	0–1	1.06	0.97	1.16
Step 2 males	0–3	1.07	0.97	1.19
Step 3 males	0–5	1.05	0.93	1.18
Step 4 males	0–10	1.07	0.78	1.46
Step 5 males	0–15	1.09	0.91	1.32

* p Value<0.05

for the low number of cases (133 ED visits) with females=105 and male=28. They show the following results. For females: step 1 (lag time 0–1), RR 1.17, CI 1.06–1.31; step 2 (lag time 0–3), RR 1.22, CI 1.081.38; step 3 (lag time 0–5), RR 1.27, CI 1.11–1.46; and step 4 (lag time 0–10), RR 1.42, CI 1.01–2.01. For males: step 1 (lag time 0–1), RR 1.06, CI 0.97–1.16; step 2 (lag time 0–3), RR 1.07, CI 0.97–1.19; and step 3 (lag time 0–5), RR 1.05, CI 0.93–1.18. For more overview, Tables 5 and 6 reported the results of the entire modeling. Figs. 1 (a and b), 2 (a and b), and 3 (a and b) show three graphic representations of RR and CRR (lag range 0–5, ED count, females and

Table 6 Results DLNM age group and specific age for sex in three classes—RR with a 5 °C unit increase in T_{mean}

Lag steps	Age groups	Lag ranges	RR	95 % CI low	95 % CI high
MOD[a]					
Step 1	19–44	0–5	1.16	1.02	1.33*
Step 1	45–65	0–5	1.05	0.90	1.21
Step 1	>65	0–5	1.25	0.95	1.64
Step 2	19–44	0–10	1.25	1.05	1.47*
Step 2	45–65	0–10	1.04	0.87	1.26
Step 2	>65	0–10	1.26	0.89	1.77
Step 3	19–44	0–15	1.20	0.99	1.48
Step 3	45–65	0–15	1.07	0.84	1.34
Step 3	>65	0–15	1.41	0.93	2.14
MOD[b]					
Step 1 females	19–44	0–1	1.13	0.99	1.30
Step 1 females	45–65	0–1	0.18	0.96	1.47
Step 1 females	>65	0–1	1.48	1.05	2.11*
Step 2 females	19–44	0–3	1.17	1.005	1.37*
Step 2 females	45–65	0–3	1.20	0.94	1.54
Step 2 females	>65	0–3	1.54	1.02	1.31*
Step 3 females	19–44	0–5	1.24	1.04	1.47*
Step 3 females	45–65	0–5	1.19	0.90	1.56
Step 3 females	>65	0–5	1.55	0.99	2.44
Step 4 females	19–44	0–10	1.35	1.08	1.68*
Step 4 females	45–65	0–10	1.23	0.87	1.75
Step 4 females	>65	0–10	1.29	0.73	2.29
Step 5 females	19–44	0–15	1.30	0.99	1.70
Step 5 females	45–65	0–15	1.27	0.82	1.95
Step 5 females	>65	0–15	1.67	0.83	3.36
MOD[c]					
Step 1 males	19–44	0–1	1.14	0.99	1.33
Step 1 males	45–65	0–1	0.96	0.84	1.10
Step 1 males	>65	0–1	1.19	0.91	1.59
Step 2 males	19–44	0–3	1.12	0.95	1.32
Step 2 males	45–65	0–3	1.02	0.87	1.20
Step 2 males	>65	0–3	1.09	0.80	1.48
Step 3 males	19–44	0–5	1.08	0.90	1.31
Step 3 males	45–65	0–5	0.99	0.83	1.19
Step 3 males	>65	0–5	1.10	0.78	1.55
Step 4 males	19–44	0–10	1.14	0.90	1.44
Step 4 males	45–65	0–10	0.98	0.78	1.22
Step 4 males	>65	0–10	1.25	0.80	1.95
Step 5 males	19–44	0–15	1.12	0.84	1.49
Step 5 males	45–65	0–15	0.99	0.75	1.31
Step 5 males	>65	0–15	1.28	0.75	2.20

* p Values<0.05

[a] Model steps with age groups

[b] Model steps with only females

[c] Model steps with only males

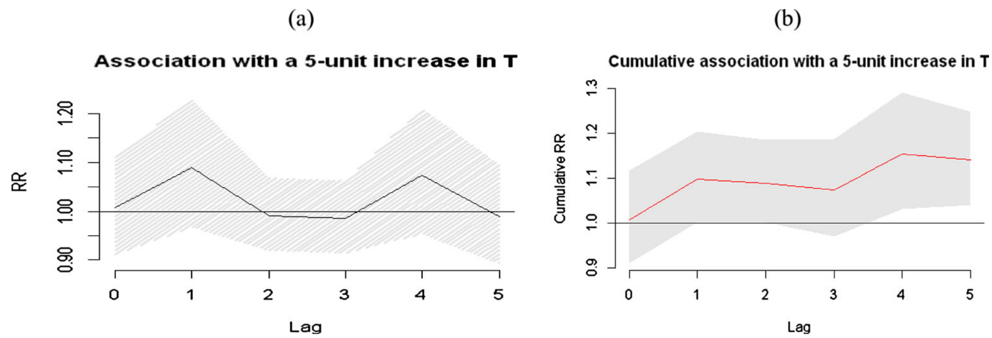

Fig. 1 **a**, **b** Relative risk (RR) and commulative RR (CRR)—association with a 5 °C unit increase in *T* (lags 0–5) for ED visits

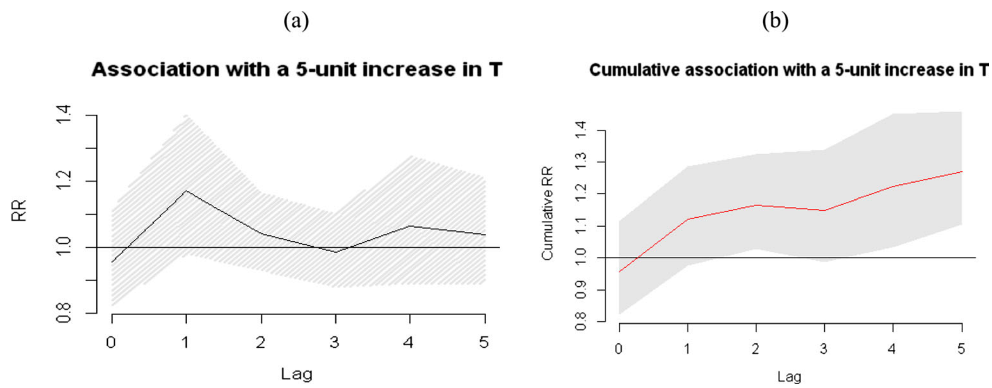

Fig. 2 **a**, **b** Relative risk (RR) and commulative RR (CRR)—association with a 5 °C unit increase in T—females (lag range 0–5)

males). The sequencing of the modeling carried suggested a weak but clear dose–response up the lag range 0–5, RR constantly >1 and low CI>1. There was also a second weak peak in the lag range 5–15 exclusively for females while no association is shown for male sex. The analysis conducted on subgroups of age revealed, for females, a significant association in the age groups 19–44, lag ranges 0–3, 0–5, and 0–10; the age group>65 years show significant RR association in the lag ranges 0–1 and 0–3 (Table 6).

The DLNM statistical modeling (stage 2) performed for subgroups of the resident population visits to ED revealed no notable differences compared to the output of the previous models (all total ED count, females and males). The bidimensional analysis plot (statistical stage 3) has shown in Fig. 4, a, b, c and d, for males and females, lag ranges 0–5 and 0–15. A representation of lag response curves for females and males are shown in Figs. 5a and b, 6a and b, and 7a and b. The sensitivity analysis results (statistical stage 4) confirm a statistically significant association for females varying the parameters of the model, with a progressive RR increase in relation to an increase of the different perturbation terms included in the sensitivity modeling. For example, in females, threshold 3 °C, RR 1.13, CI 1.05–1.21 and threshold 7 °C (time $9^{*}4$) and lag range 0–3, RR 1.29, CI 1.11–1.50 (Table 7). No effect was confirmed for males.

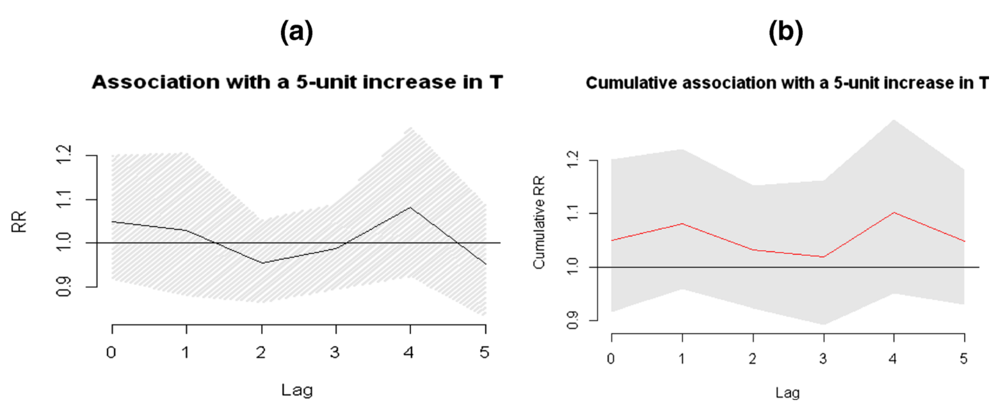

Fig. 3 **a**, **b** Relative risk (RR) and commulative RR (CRR)—association with a 5 °C unit increase in T—males (lag range 0–5)

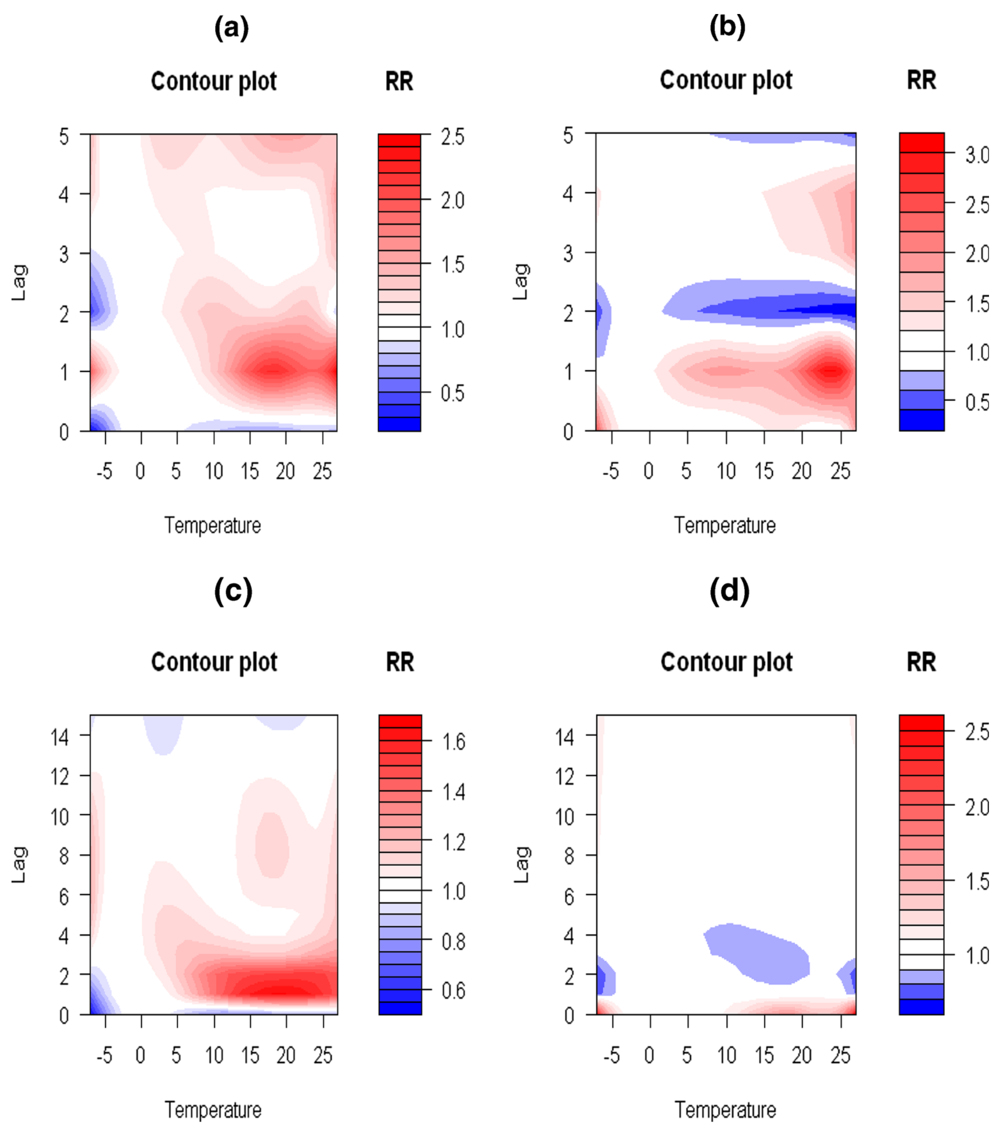

Fig. 4 Bidimensional dlnm exposure—lag response association (lags 0–5)—contour plot females (**a**, **c**) and males (**b**, **d**)

Discussion

The climatological data of Cuneo show a clear consistency with the global thermometric data used for comparison here (GissTemp and HadCRU), with a greater increase of the temperature registered in the last two decades. The statistical results show a clear association between the thermal component and the onset of RC and UC. This evidence was important in the first modeling (stage 1), which includes only the weather–climate components adjusted for seasonal and long-term trend, and other confounding factors. We did not observed statistically significant associations with hygrometric, pyranometric, and pressure measures (p value<0.05). In particular, RH, TR, and pressure do not show any statistically significant association. The model adjusted for seasons and calendar days still shows an association between T_{mean} and the RC and UC, although moderate. This data seems only partly in agreement with previous research (Cervellin et al. 2011). In particular, concerning relative humidity, the estimation of Poisson model (stage 1) and the application of dose–response model (PGAM with DLNM—stage 2) do not show statistically significant associations between relative humidity and incidence of RC (Cervellin et al. 2012) with CI constantly low at <1 (RR in several steps <1). In our opinion, it is necessary to carry out further research to confirm or refute this result.

This could be explained by taking into account an aspect not considered in the previous literature: the altimetric profile of the places studied. In fact, the existence of a vertical temperature profile (vertical thermal gradient), with a decrease of 0.6–1 °C/100-m height, could play a role. This hypothesis needs to be further investigated and compared to other results, but it seems to suggest a different RR profile, according to the altitude-related climatic conditions.

Analysis carried out to estimate the lagged effects (dose–response) classified according to sex, age, age and sex, Cuneo City (included neighboring towns) and all other

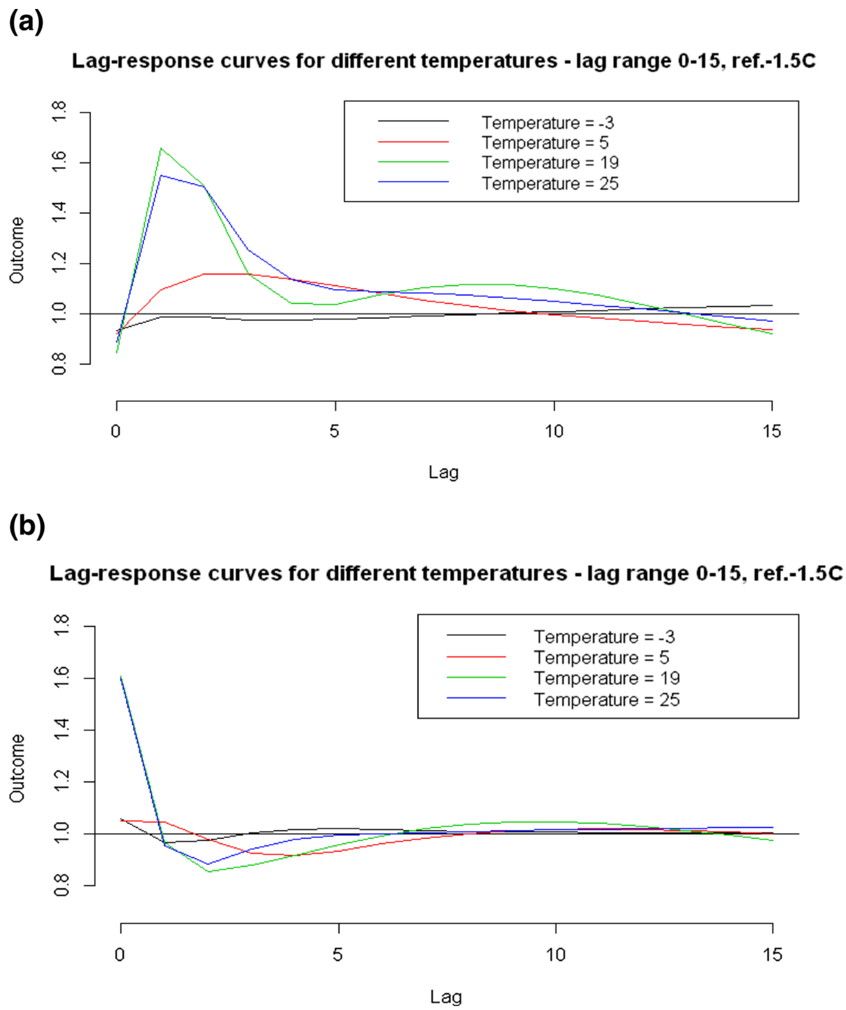

Fig. 5 Bidimensional dlnm (lags 0–15)—lag response curves females (**a**) and males (**b**)

municipalities showed a significant association of RR in the overall model (lag ranges 0–1 and 0–3) and, for females, mainly in the lag ranges 0–1, 0–3, and 0–5 ($p>0.05$). On the contrary, no significance was observed for the male sex ($p<0.05$). The bidimensional analysis shows a higher concentration in the RR, lag range 0–5, for females, and a modest RR for males in the lag range 0–1. The effect shown in the lag range 10–15, exclusively for females, is probably a bounce of the spline functions, which is created by their relative inflexibility. Therefore, more research is needed to confirm this result.

The research has some limitations since it would be necessary to consider and add in the statistical model other potential etiological factors in addition to the climate variables. It has been described that a diet rich in animal protein could be associated to an increased risk of UC. The mechanism has been correlated to an increased urinary calcium excretion and a decreased excretion of citrate (Taylor et al. 2004; Curhan et al. 2004). Obesity has also been considered an independent risk factor in the onset of UC and both body mass index (BMI) and waist circumference measures resulted to be strongly associated (Taylor et al. 2005). An increased risk of preterm birth in women hospitalized for UC was also described, with an estimated incidence of 1.7 per 1,000 accesses (Swartz et al. 2007).

Hypertension was, in turn, explored as a risk factor for RC, with a prevalence in obese women but not in men (Gillen et al. 2005).

Also type II diabetes seems to be associated with nephrolithiasis via mechanisms including increased production of uric acid, insulin resistance, and low pH (Lieske et al. 2006; Eisner et al. 2010). The prevalence of diabetes observed in our study in the male sex (74.5 %) could be explained, according to a previous study (Lieske et al. 2006) by considering that the basal higher level of uric acid in these patients could play as an additional pathogenetic factor of RC.

Other studies also reported an association between UC and metabolic syndrome (West et al. 2008). It would thus be important to perform new studies including both the climate variables and other covariates abovedescribed, which may be important additional risk factors.

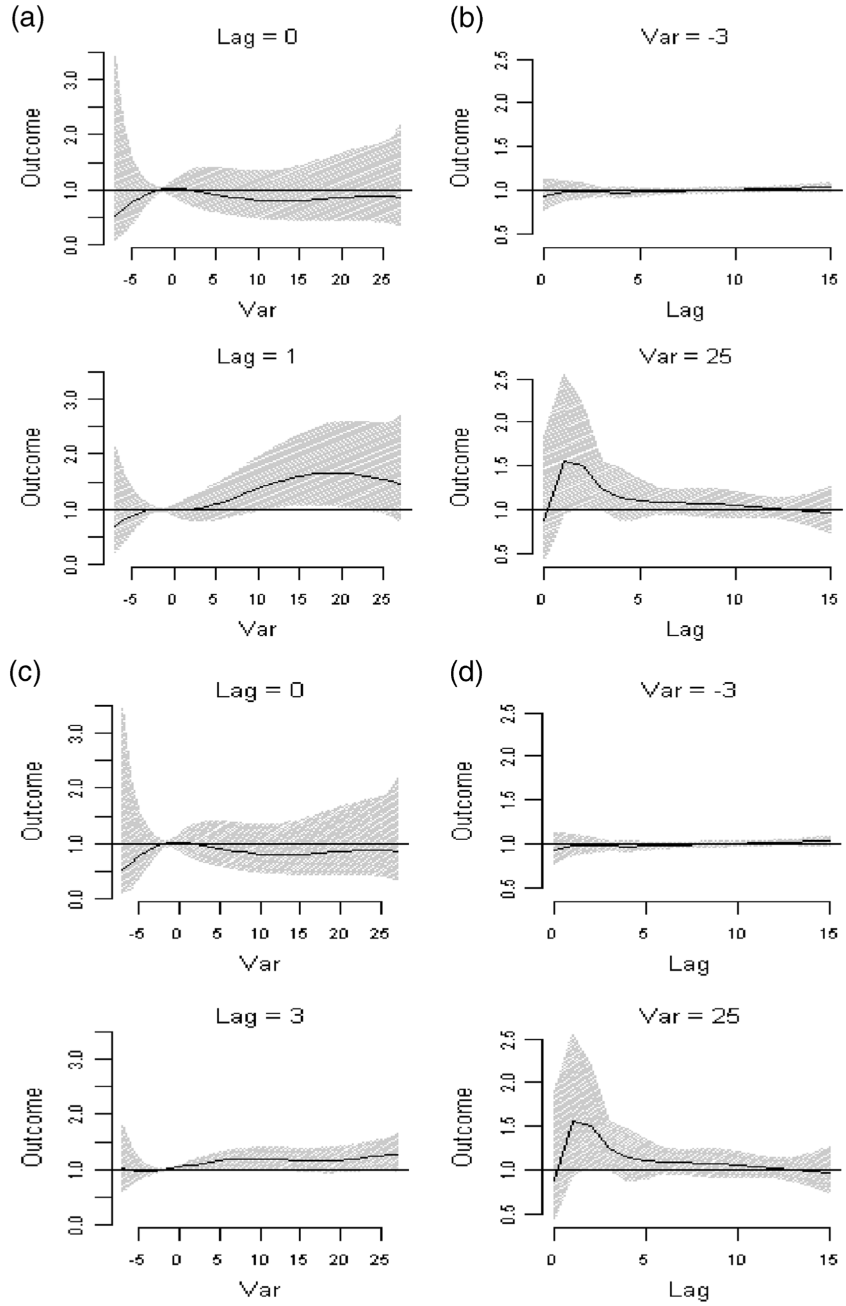

Fig. 6 Bidimensional dlnm (lags 0–15)—lag response curves for females (**a** and **b**) at lags 0–1 and 0–3, respectively

The aim of this study was to connect the medical bioclimatology to aspects of preventive medicine. The water–salt balance is influenced by several factors (environment, climate, diet, metabolism, physical activity, etc.) and is regulated by a strong interconnection between the hormonal, renal, and neurological systems, with kidney playing a major role through glomerular ultrafiltration and tubular reabsorption and secretion. One of the most important factors affecting the renal system is the daily water intake. If properly consumed, water may prevent urine supersaturation, which is the most important contributor in pathogenesis of UC especially occurring in conditions of increased temperatures and may inhibit the central secretion of antidiuretic hormone (ADH) thus increasing polyuria.

On the basis of the meteo-climatological characteristics of the area considered in the study, our data suggest that a proper hydration is an important strategy to prevent RC and an education program could be a useful tool to achieve this goal.

The water supply, in respect of the absence of medical contraindications, should respect the parameters of quantity, already mentioned in the guidelines (production of at least 2 l of urine/day in case of high physical activity; 1 ml

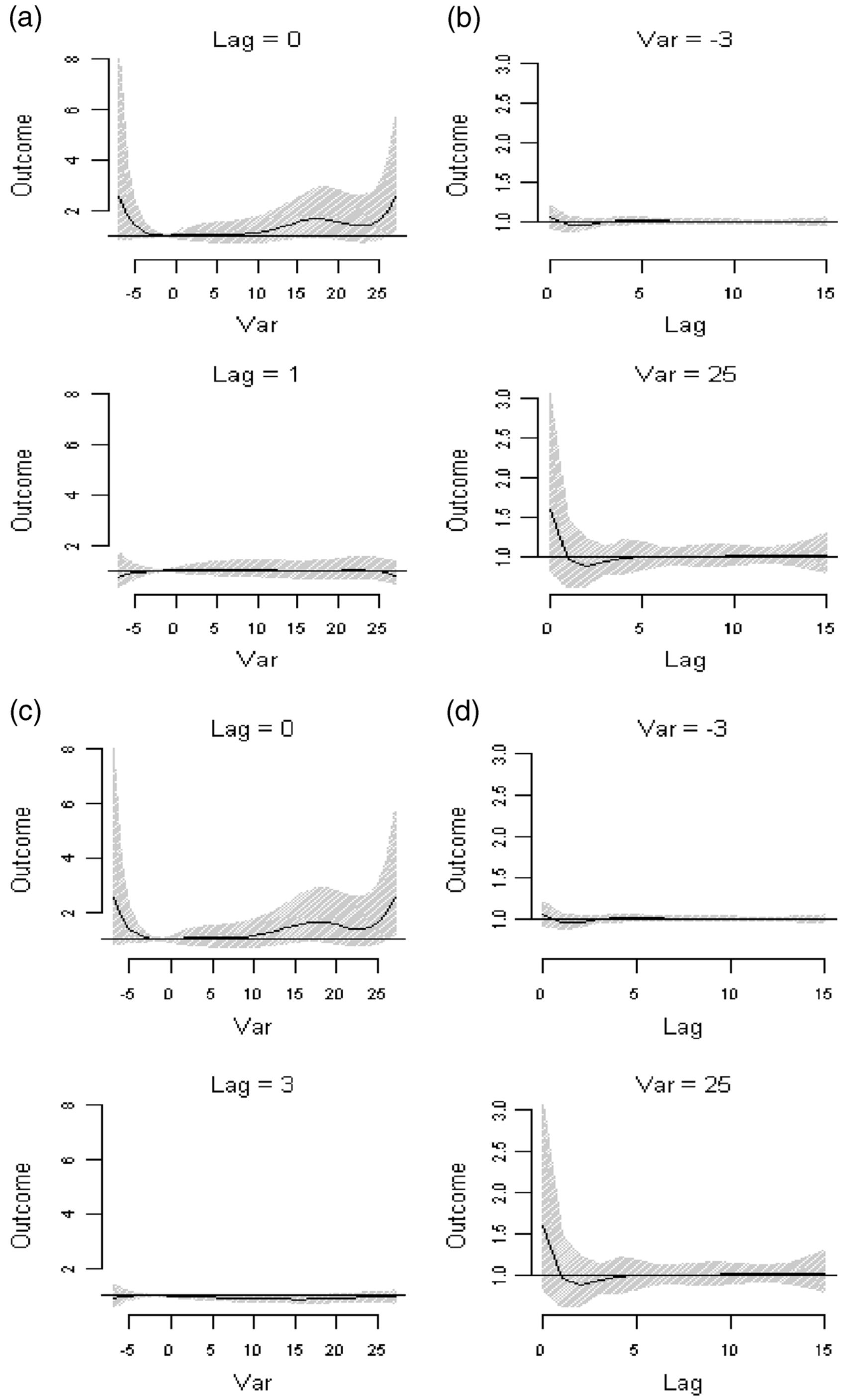

Fig. 7 Bidimensional dlnm (lags 0–15)—lag response curves for males (**a** and **b**) at lags 0–1 and 0–3, respectively

of water/cal/day but never less than 1 l/day; Borghi et al. 1996, 2006; Cuhran 2007). Finally, as already described in previous papers (Boscolo-Berto et al. 2008), water consumption should also be modified according to monthly and seasonal T_{mean} and T_{max}.

In addition, our data indicated that the altitude could be a protective factor in the onset of RC and that particular attention should be given to the female sex in terms of prevention.

Regarding the analysis of ED visits, it seems necessary to structure a study model with properties of homogeneity. In this way, it will be possible, in the future, to program meta-analytic approaches comparable for geographical areas relatively homogeneous. In conclusion, our study intends to focus the attention of the researchers on issues related to inclusion/exclusion criteria, indicating a thorough methodology in compiling the ED database in order to minimize possible factors of distortion associated to the diseases studied.

Table 7 Sensitivity analisys (daily number ED and ED females visits)

T_{mean}[a] (°C)	*df* (time)	Lag ranges	RR ED visits	95 % CI low ED visits	95 % CI high ED visits	RR ED visits females	95 % CI low ED visits females	95 % CI high ED visits females
3	6*4	0–3	1.08	1.03	1.31*	1.13	1.05	1.21*
3	8*4	0–3	1.09	1.03	1.14*	1.13	1.05	1.22*
3	9*4	0–3	1.09	1.04	1.15*	1.14	1.05	1.22*
3	6*4	0–5	1.08	1.03	1.14*	1.16	1.07	1.26*
3	8*4	0–5	1.09	1.04	1.15*	1.17	1.07	1.27*
3	9*4	0–5	1.10	1.04	1.16*	1.17	1.08	1.26*
4	6*4	0–3	1.11	1.04	1.18*	1.17	1.06	1.29*
4	8*4	0–3	1.12	1.05	1.19*	1.18	1.07	1.31*
4	9*4	0–3	1.12	1.05	1.20*	1.19	1.07	1.31*
4	6*4	0–5	1.11	1.04	1.20*	1.22	1.09	1.35*
4	8*4	0–5	1.13	1.05	1.21*	1.23	1.10	1.37*
4	9*4	0–5	1.14	1.06	1.22*	1.24	1.10	1.38*
6	6*4	0–3	1.16	1.06	1.28*	1.27	1.10	1.47*
6	8*4	0–3	1.18	1.07	1.30*	1.28	1.11	1.49*
6	9*4	0–3	1.19	1.08	1.32*	1.29	1.11	1.50*
6	6*4	0–5	1.17	1.06	1.31*	1.34	1.14	1.58*
6	8*4	0–5	1.20	1.07	1.34*	1.36	1.15	1.61*
6	9*4	0–5	1.21	1.09	1.35*	1.37	1.16	1.63*
7	6*4	0–3	1.19	1.07	1.33*	1.32	1.12	1.58*
7	8*4	0–3	1.21	1.08	1.36*	1.34	1.12	1.59*
7	9*4	0–3	1.23	1.09	1.38*	1.35	1.13	1.61*
7	6*4	0–5	1.21	1.06	1.36*	1.41	1.16	1.70*
7	8*4	0–5	1.24	1.09	1.40*	1.43	1.18	1.74*
7	9*4	0–5	1.25	1.10	1.45*	1.45	1.19	1.76*
5[b]	7*4	0–3	1.14	1.05	1.23*	1.22	1.09	1.38*
5[b]	7*4	0–5	1.15	1.05	1.25*	1.28	1.11	1.47*

* p Value≤0.05

[a] Temperature increment

[b] Baseline model

Acknowledgments We would like to thank Hospital S. Croce and Carle of Cuneo for data and Mrs. Olivia Cerrina and Mr. Mauro Giraudo for their assistance during the research.

Conflict of interest There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

References

Al-Hadramy MS (1997) Seasonal variations of urinary stone colic in Arabia. J Pak Med Assoc 47:281–284

Altan L, Andreoni C, Ortiz V, Koga ES, Pitta R, Atan F, Srougi M (2005) High kidney stone risk in men working in steel industry at hot temperatures. Urology 65:858–861

Association of Italian Urologists (2007) Guideline on urinary stones

Ballester F, Corella D, Perez-Hoyos S, Saez M, Hervas A (1997) Mortality as a function of temperature. A study in Valencia, Spain, 1991–1993. Int J Epidemiol 26:551–561

Besancenot JP (2002) Vagues de chaleur et mortalité dans les grandes agglomérations urbaines. Environ Risques Santé 1:229–240

Bhaskaran K, Gasparrini A, Hajat S, Smeeth L, Armstrong B (2013) Time series regression studies in environmental epidemiology. Int J Epidemiol 42(4):1187–1195

Borghi L, Ferretti PP, Elia GF et al (1990) Epidemiological study of urinary tract stones in a northern Italian city. Br J Urol 65:231–235

Borghi L, Meschi T, Amato TF et al (1996) Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a five-year randomized prospective study. J Urol 155:839–843

Borghi L, Meschi T, Maggiore U, Prati B (2006) Dietary therapy in idiopathic nephrolithiasis. Nutr Rev 64(7):301–312

Boscolo-Berto R, Dal Moro M, Abate A, Arandjelovic G, Tosato F, Bassi P (2008) Do weather conditions influence the onset of renal colic? A novel approach to analysis. Urol Int 80:19–25

Brikowsky TH, Lotan Y, Pearle MS (2008) Climate-related increase in the prevalence of urolithiasis in the United States. PNAS 105:9841–9846

Cervellin G, Comelli I, Comelli D, Cortellini P, Lippi G, Meschi T, Borghi L (2011) Regional short-term climate variation influence on the number of visits for renal colic in a large urban emergency department: results of a 7-year survey. Intern Emerg Med 6:141–147

Cervellin G, Comelli I, Comelli D, Meschi T, Lippi G, Borghi L (2012) Mean temperature and humidity variations, along with patient age, predict the number of visits for renal colic in a large urban emergency department: results of a 9-year survey. J Epidemiol Glob Health 2:31–38

Chen Y, Lin H, Chen C et al (2008) Seasonal variations in urinary calculi attacks and their association with climate: a population based study. J Urol 179:564–569

Cuhran GC (2007) Epidemiology of stone disease. Urol Clin N Am 34(3):287–293

Curhan GC, Willett WC, Knight EL, Stampfer MJ (2004) Dietary factors and the risk of incident kidney stones in younger women: nurses' health study II. Arch Intern Med 164:885–891

Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA (2002) Temperature and mortality in 11 cities of the eastern United States. Am J Epidemiol 155:80–87

Curtin J, Sampson M (1989) Greenhouse effect and renal calculi. Lancet 2:1110

Dessai S (2002) Heat stress and mortality in Lisbon: Part 1. Model construction and validation. Int J Biometeorol 47:6–12

Dessai S (2003) Heat stress and mortality in Lisbon: Part II. An assessment of the potential impacts of climate change. Int J Biometeorol 48:37–44

Eisner BH, Porten SP, Bechis SK et al (2010) Diabetic kidney stone formers excrete more oxalate and have lower urine pH than nondiabetic stone formers. J Urol 183:2244–2248

Evans K, Costabile RA (2005) Time to development of symptomatic urinary calculi in a high-risk environment. J Urol 173:858–861

Fakheri RJ, Goldfarb DS (2011) Ambient temperature as a contributor to kidney stone formation: implications of global warming. Kidney Int 79:1178–1185

Fujita K (1987) Weather and the incidence of urinary stone colic in Tokyo. Int J Biometeorol 31:141–146

Gasparrini A (2011) Distributed lag linear and non-linear models in R: the package dlnm. J Stat Softw 43(8):1–20

Gillen DL, Coe FL, Worcester EM (2005) Nephrolithiasis and increased blood pressure among females with high body mass index. Am J Kidney Dis 46:263–269

Goggins WG, Woo J, Ho S, Chan EYY, Chau PH (2012) Weather, season, and daily stroke admission in Hong Kong. Int J Biometeorol 56:865–872

Guo Y, Punnasiri K, Tong S (2012) Effects of temperature on mortality in Chiang Mai City, Thailand: a time series study. Environ Health 11:36. doi:10.1186/1476-069X-11-36

Hu W, Mengersen K, Mc Michael A, Tong S (2008) Temperature, air pollution and total mortality during summer in Sydney, 1994–2004. Int J Biometeorol 52:689–696

Hussain F, Billimoria FR, Singh PP (1990) Urolithiasis in northeast Bombay: seasonal prevalence and chemical composition of stones. Int Urol Nephrol 22:119–124

Collana di Studi Climatologici in Piemonte (1998) Regione Piemonte. Dip. di Scienze della Terra, Università degli Studi di Torino

IPCC4 (2007) Climate change 2007: the physical science basis, summary for policymakers. Fourth climate assessment report. UN Intergovernmental Panel on Climate Change, Geneva, pp 1–18

Johnson H, Griffiths C (2003) Estimating excess winter mortality in England and Wales. Health Stat Q 20:19–24

Kovats SR, Hajat S, Wilkinson P (2004) Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in greater London, UK. Occup J Environ Med 61:893–898

Lieske JC, de la Vega LS, Gettman MT, Slezak JM, Bergstralh EJ, Melton LJ, Leibson CL (2006) Diabetes mellitus and the risk of urinary tract stones: a population-based case-control study. Am J Kidney Dis 48:897–904

Makle T, Harada M, Kinukawa N, Tojoshiba H, Yamanaka T, Nakamura T, Sakamoto M, Nose Y (2001) Association of meteorological factors and day of the week with emergency hospital admissions in Fukuoka. Japan. Int J Biometeorol 46:38–41

Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, Biggeri A, Ross Andeson H, Katsouyanni K, Ballester F, Bisanti L, Cadum E, Forsberg F, Forastiere F, Goodman PG, Hojs A, Kirchmayer U, Medina S, Paldy A, Schindler C, Sunyer J, Perucci CA (2009) High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. Am J Respir Crit Care Med 179:383–389

Nastos PT, Matzarakis A (2006) Weather impacts on respiratory infections in Athens, Greece. Int J Biometeorol 50:358–369

Peterson TC, Easterling DR (1994) Creation of homogeneous composite climatological reference series. Int J Climatol 14:691–679

Pierce LW et al (1945) Observations on urolithiasis among American troops in a desert area. J Urol 54:466–476

Revich B, Shaposhnilkov D (2008) Temperature-induced excess mortality in Moscow. Int J Biometeorol 52:367–374

Robertson WG, Peacock M, Marshall RW et al (1975) Seasonal variations in the composition of urine in relation to calcium stone-formation. Clin Sci Mol Med 49:597–602

Rusticucci M, Bettolli ML (2002) Association between weather condition and the number of patients at the emergency room in an Argentine hospital. Int J Biometeorol 46:42–51

Schwartz J (2000) The distributed lag between air pollution and daily deaths. Epidemiology 11(3):320–326

Semenza JC, Rubin CH, Falter KH, Selanikio JD, Flanders WD, Howe HL, Wilhelm JL (1996) Heat-related deaths during the July 1995 heat wave in Chicago. N Engl J Med 335:84–90

Soucie JM, Coates RG, McClellan W, Austin H, Thun M (1996) Relation between geographic variability in kidney stones prevalence and risk factors for stones. Am J Epidemiol 143:487–495

Stafoggia M, Forastiere F, Agostini D, Biggeri A, Bisanti L, Cadum E, Caranci N, De' Donato F, De Lisio S, de Maria M, Michelozzi P, Miglio R, Pandolfi P, Picciotto S, Rognoni M, Russo A, Scarnato C, Perucci CA (2006) Vulnerability to heat-related mortality: a multicity population-based case-crossover analysis. Epidemiology 17:315–323

Swartz MA, Lydon-Rochelle MT, Simon D, Wright JL, Porter MP (2007) Admission for nephrolithiasis in pregnancy and risk of adverse birth outcomes. Obstet Gynecol 109:1099–1104

Taylor EN, Stampfer MJ, Curhan GC (2004) Dietary factors and the risk of incident kidney stones in men: insights after 14 years of follow-up. J Am Soc Nephrol 15:3225–3232

Taylor EN, Stampfer MJ, Curhan GC (2005) Obesity, weight gain, and the risk of kidney stones. JAMA 293:455–462

Thirion X (1992) La vague de chaleur de juillet 1983 à Marseille: enquête sur la mortalité, essai de prévention. Santé Publique 4:58–64

West B, Luke A, Durazo-Arvizu RA et al (2008) Metabolic syndrome and self-reported history of kidney stones: the National Health and Nutrition Examination Survey (NHANES III) 1988–1994. Am J Kidney Dis 51:741–747

Yu W, Mengersen K, Wang X, Ye X, Guo Y, Pan X, Tong S (2012) Daily average temperature and mortality among the elderly: a meta-analysis and systematic review of epidemiological evidence. Int J Biometeorol 56:569–581