



Contents lists available at ScienceDirect

Allergy International

journal homepage: <http://www.elsevier.com/locate/alit>

Original article

Cross sectional questionnaire-based internet study: Self-perception and clinical course of drug allergy in Greece

Michael P. Makris^{a,*}, Theodoros N. Sergentanis^b, Xenophon Aggelides^a,
Stamatios Tzanninis^b, Efthimia Polyzou^a, Dimitrios Rigopoulos^a,
Theodora Psaltopoulou^b

^a Allergy Unit 'D. Kalogeromitros', 2nd Department of Dermatology and Venereology, Medical School, National and Kapodistrian University of Athens, "Attikon" University Hospital, Athens, Greece

^b Department of Hygiene, Epidemiology and Medical Statistics, Medical School, National and Kapodistrian University of Athens, Athens, Greece

ARTICLE INFO

Article history:

Received 3 April 2016

Received in revised form

24 April 2016

Accepted 28 April 2016

Available online xxx

Keywords:

Allergy

Drug hypersensitivity

Internet

Risk factors

Survey

Abbreviations:

ADR Adverse drug reaction

OR odds ratio

ABSTRACT

Background: Data on self perception of drug allergy in the general population are lacking. Epidemiological studies focus either on specific populations or document adverse drug reactions in general. Our objective was to document self-reported drug allergy in Greece, through a simple, informative internet-based questionnaire.

Methods: A questionnaire on drug allergy was accessible online for a 3-month period. Participants voluntarily answered 28 questions referring to: suspected drug, clinical manifestations, concomitant factors, received treatment, reaction's re-occurrence.

Results: A total of 2528 questionnaires were included in study analysis. Beta-lactams and non-steroidal anti-inflammatory drugs were the most prevalent culprit agents (53% and 27.5% respectively) while half of the participants acknowledged skin manifestations as the most common symptoms. One out of three reported subsequent exposure to the drug presumed to be responsible for the reaction and 74.5% of those stated a new reaction upon re-exposure. Only 26.7% underwent allergological evaluation. Reactions manifested with respiratory or cardiovascular symptoms, parenteral administration of the culprit drug and personal history of allergy to agents of >1 different pharmacological categories were associated with increased risk of hospitalization.

Conclusions: Allergic reactions to drugs are adverse events difficult to define and diagnose. A remarkable proportion of presumed as hypersensitivity reactions are not referred to allergists; therefore these patients may be either re-exposed to potentially noxious drugs, or needlessly avoid whole classes of drugs as b-lactams for more costly or less appropriate treatments. Internet-based questionnaires may contribute to awareness programs concerning drug allergy and help improve proper referral.

Copyright © 2016, Japanese Society of Allergy. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Adverse drug reactions (ADRs) account for 3–6% of hospital admissions while their prevalence among hospitalized patients is estimated between 10 and 15%. ADRs represent a major health problem with increased morbidity, prolonged hospitalization and risk of mortality. According to the World Health Organization, an ADR is defined as “a response to a medicine which is noxious and

unintended, and which occurs at doses normally used in man”.¹ Furthermore ADRs are divided in Type A that are predictable and dose-dependent and Type B that are unpredictable, dose independent and comprise 15–20% of all ADRs. The latter group includes both immunologically mediated drug hypersensitivity (alternatively called drug allergy) and non-immune mediated reactions.¹

Although drug allergy is of major importance, its true incidence and other epidemiological features are not well studied. The vast majority of epidemiologic data refers rather to ADRs than to drug allergy specifically.² Besides, a great confusion about drug allergy exists among health care providers and patients. Previous studies reported a large number of medication errors and hospital admissions due to allergic reactions attributed to drugs in outpatient

* Corresponding author. Allergy Unit “D. Kalogeromitros”, “Attikon” University Hospital, 1 Rimini str, Haidari, PC 12462, Athens, Greece.

E-mail address: mmakris.allergy@gmail.com (M.P. Makris).

Peer review under responsibility of Japanese Society of Allergy.

<http://dx.doi.org/10.1016/j.alit.2016.04.016>

1323–8930/Copyright © 2016, Japanese Society of Allergy. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

settings.³ It is likely that only the more severe and/or complex cases are referred to specialists and therefore only in these cases the diagnosis is well documented; thus studies that use clinical questionnaires for addressing drug allergy may not present the “real life” situation.

Internet portals have created new opportunities for the assessment of numerous medical conditions. Internet-based questionnaires encourage a greater number of individuals from a broad geographic area to take part providing thus the opportunity to perform wide scale surveys by overcoming traditional problems like high financial costs. Information transmitted via secure portals could allow for the identification of chronic problems even better than visits to non-specialists in these medical entities. Based on this information, the web-users can provide important data about certain medical conditions that reflect the patients' perception about their own problem. However, a selection bias to internet-users exclusively and self-reporting are potential limitations. Our previous experience with internet surveys was very positive as we revealed interesting aspects about the patients' perspective and the way they handle disease.^{4,5}

We have conducted this study in order to record self perception of drug allergy among internet users in Greece. Secondary goals of the study were the assessment of management of these conditions, the compliance of patients to the advice provided by treating physicians, as well as the identification of risk factors for severe reactions.

Methods

Study design

A specific questionnaire (Supplementary Table 1) on drug allergy was generated by Drug Allergy Outpatient Clinic, Allergy Unit, Attikon General University Hospital, Athens, Greece. Subsequently, the questionnaire, consisted of 28 questions, was placed on the website of <http://www.in.gr>, one of the most reliable online information portals in Greece which includes a popular “health zone” through distinguished links placed on this site. All online visitors with personal history of drug allergy were invited to take part in the study through an introductory page. The questionnaire was posted by Internet portal for a 3-month period. Each participant could fill the questionnaire only once; to this end, a safety feature of the website prohibited voting from the same IP address more than once. Individuals without a history of drug allergy were excluded from the study by an introductory screening question (No 6, Supplementary Table 1). Demographic data including age, gender and address zip code of participants were also collected. Participants younger than 12 years were excluded from data analysis. Study subjects participated anonymously and the introductory page clearly stated that the obtained data would be used for epidemiological research only. After study analysis, the most important results and conclusions as well as general information and recommendations for drug allergy sufferers, were posted at the same portal.

The protocol was approved by the Ethics Committee of Attikon University Hospital.

Statistical analysis

Statistical analysis consisted of two steps. First, descriptive statistics were calculated. Continuous variables are presented as mean values $\pm$ standard deviation (SD), whereas categorical variables are presented as absolute and relative frequencies. Secondly, potential risk factors were evaluated along three main axes: (i) hospitalization; (ii) repeated intake of the allergenic drug after the first

reaction; and (iii) reported subsequent specific allergological evaluation with skin testing. Multivariate logistic regression was performed; the factors that were significantly associated with the aforementioned items at the univariate analysis were examined as independent variables.

In the final model, after mutual adjustment, only the statistically significant variables were included (backward selection statistical procedure). Similarly to our previous work,⁵ a hierarchical approach was adopted concerning the modeling of the three axes. The underlying conceptual framework envisaged the time succession: first (serious) reaction $\rightarrow$ hospitalization $\rightarrow$ non-compliance with medical advice (repeated intake of the allergenic drug after the reaction) or compliance with medical advice (and allergological evaluation with skin testing). Consequently, the model for repeated intake also encompassed hospitalization as an independent variable, whereas the model concerning skin testing examined both hospitalization and subsequent intake of the culprit drug.

Symptoms were grouped according to the affected organ and system: upper (nasal congestion, runny nose, sneezing, ocular itch and or hemosis of conjunctiva) and lower respiratory system (chest tightness, wheezing, dry cough, voice hoarseness), skin (urticaria – angioedema, maculopapular exanthema, itching, generalized flushing), cardiovascular (tachycardia, dizziness, loss of consciousness), gastrointestinal (abdominal pain, diarrhea, vomiting) and

Table 1
Descriptive characteristics of study participants.

Variables	N (%)
Male sex	762 (30.3)
Education	
Primary (6 years)	67 (2.7)
Secondary (9 years)	67 (2.7)
High school (12 years)	844 (33.9)
University	1512 (60.7)
Age at first reaction (years)	
0–10	299 (11.9)
11–20	446 (17.8)
21–30	818 (32.6)
31–40	444 (17.7)
41–50	220 (8.8)
51–60	124 (4.9)
>60	157 (6.3)
Administration of the culprit drug by injection (IM or IV)	312 (12.4)
Occurrence of the reaction at home	2225 (89.4)
Time interval between drug intake and symptoms' onset	
1–3 h	1292 (51.7)
3–72 h	799 (32.0)
>72 h after the initiation of treatment	361 (14.4)
After the completion of treatment	49 (2.0)
Hospitalization	989 (39.4)
Duration of symptoms	
<4 h	1095 (43.7)
1–7 days	1119 (44.6)
>7 days	293 (11.7)
Repeated intake of the culprit drug	737 (29.3)
Co-existing factors	1254 (49.6)
History of allergy to agents of >1 different pharmacological categories	782 (31.5)
Personal history of atopy (allergic rhinitis, asthma, atopic dermatitis)	1303 (51.5)
Family history of atopy (first-degree relative)	1123 (48.0)
Previous surgery	1242 (49.5)
Chronic concomitant diseases	342 (13.9)
Allergological evaluation with skin testing	666 (26.7)
Treating physician	
No evaluation at all	854 (34.3)
Allergist	574 (23.0)
Other than allergist	1065 (42.7)

other. Co-existing triggering factors were treated as a binary variable i.e. any (stress, exercise, infection, fever) vs. none. Regarding the follow-up of patients, the distinction was made between consultation by an allergist or specialist on other specialties (dermatology, internal medicine or general practice) and non-medical consultation at all. The level of statistical significance was set at 0.05. All analyses were performed with STATA version 11.1 (STATA Corporation, College Station, TX, USA).

Results

Epidemiological data

The final dataset that was included in study analysis consisted of 2528 responders of a mean age 35.6 ± 11.1 years (range 12–77 years). The descriptive characteristics of the participants are presented on Table 1. The culprit drugs for the reaction according to patients' reports were: antibiotics (1297 patients, 53.0%), non-steroidal anti-inflammatory drugs (NSAIDs; 674pts, 27.5%), local corticosteroids (66pts, 2.7%), general anesthetics (62pts, 2.5%), vaccines (32pts, 1.3%), radio contrast media and fluorescein (25pts, 1.0%), local anesthetics (30pts, 1.2%), chemotherapeutic agents (6pts, 0.25%); the remaining 10.5% consisted of various other agents.

Coexisting factors were reported by 1254 patients; the most prevalent were fever ($n = 415$, 33.1%), infection ($n = 415$, 33.1%), emotional stress ($n = 396$, 31.6%) and physical exercise ($n = 28$, 2.2%).

Clinical characteristics

The clinical manifestations according to the systems' involvement are depicted on Fig. 1. The most common symptoms from different systems were: a/among 1233 subjects with skin manifestations: flushing 31.1%, urticaria $\pm$ angioedema 27.6%, maculopapular rash 22.9%, pustular or bullous rash 5.7%, sole angioedema 5.2%, generalized pruritus 3%, eczema 2.4% and exfoliate dermatitis or necrotic dermatoses 2%, b/among 413 subjects with cardiovascular symptoms: loss of consciousness 37.3%, dizziness 32.9% and tachycardia 29.8%, c/among 262 subjects with lower airways' manifestations: chest tightness 77.5%, voice hoarseness 20.2% and wheezing-dry cough 6.9%, d/among 183 subjects with gastrointestinal symptoms: nausea-vomiting 38.8%, abdominal

pain 31.1% and diarrhea 30.1%, e/among 159 subjects with upper respiratory symptoms: orbital edema 47.2%, ocular itch and/or hemosis of conjunctiva 23.9%, nasal congestion 9.4%, runny nose 3.8%. Other variable symptoms (arthralgia/myalgia, jaundice, malaise, lymphadenopathy, neuropathy, renal dysfunction) were reported by 9.4% of participants.

A high percentage of participants (737/2528, 29.3%) reported subsequent intake of the culprit drug; among them, 556 (75.4%) reported reoccurrence of allergic reaction after re-administration of the offending drug. According to reactors' perception, the reaction was less severe in 91/556 of cases (16.4%), equally severe with the prior one in 373/556 of cases (67.1%) and more severe in 92/556 (16.6%) respectively.

Multivariate analysis

The results of the multivariate logistic regression for hospitalizations are presented on Table 2. Accordingly, presence of lower respiratory symptoms (OR = 2.47) or cardiovascular symptoms (OR = 2.16), administration of the culprit drug via intravenous or intramuscular injection (OR = 1.60), history of allergic reactions to >1 agents of different pharmacological categories (OR = 1.21) were associated with increased risk for hospitalization; on the contrary, delayed onset of symptoms after drug intake (OR = 0.87), higher educational level (OR = 0.86) and occurrence of the reaction at home (OR = 0.56) were identified as protective from hospitalization.

Referring subsequent intake of the culprit drug the multivariate analysis has shown that presence of any concomitant chronic disease (OR = 1.61), male sex (OR = 1.42), reaction to Non-Steroids Anti-inflammatory Drugs (OR = 1.40), prior history of surgical procedures (OR = 1.38) and multiple reactions to different drugs (OR = 1.36) were predisposing factors for re-consumption of the culprit agent. On the other hand, history of hospitalization after previous drug allergic reaction (OR = 0.75), antibiotic allergy (OR = 0.75), as well as parenteral administration (OR = 0.65) seemed to protect from any subsequent intake of the culprit drug (Table 3).

The analysis for specific allergological evaluation with in vivo testing after the reaction is presented in Table 4. In case of vaccine suspected allergy testing was performed more frequently (OR = 2.54), as well as in case of personal history of atopy

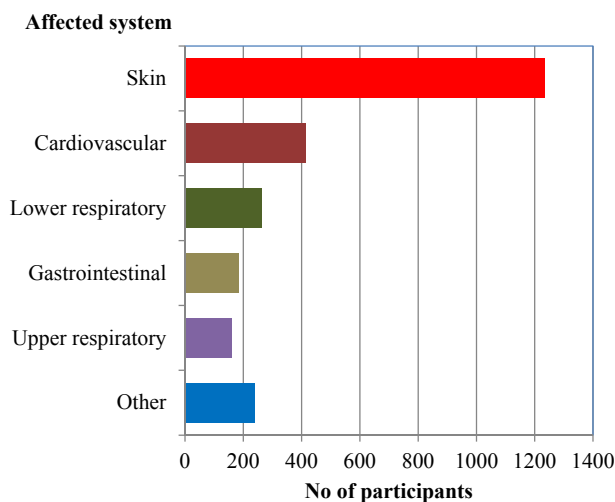


Fig. 1. Systems' involvement in the reported allergic reactions.

Table 2
Multivariate logistic regression analysis for hospitalization.

Variables retained	Category or increment	OR (95% CI)	p-value
Lower airways symptoms	Lower respiratory vs. non-cardiovascular/non-lower respiratory symptoms	2.47 (1.87–3.25)	<0.001
Cardiovascular symptoms	Cardiovascular vs. non-cardiovascular/non-lower respiratory symptoms	2.16 (1.71–2.73)	<0.001
Injected administration of the drug	Injection (IV, IM, SC) vs. all other ways of administration	1.60 (1.16–2.21)	0.004
History of allergic reactions to agents of >1 different pharmacological categories	More than one vs. one category	1.21 (1.00–1.45)	0.045
Delayed symptoms' onset	One level increase	0.87 (0.77–0.97)	0.014
Higher education	One level increase	0.86 (0.76–0.98)	0.021
Occurrence at home	Occurrence at home vs. elsewhere	0.56 (0.40–0.79)	0.001

OR, odds ratio; 95% CI, confidence interval.

(OR = 1.76); on the contrary, consultation by physicians of other specialties than allergy (OR = 0.07) or no referral to any physician after the reaction (OR = 0.02) strongly predicted lack of allergological testing.

Discussion

To our knowledge, this study represents the largest internet-based attempt to document self-reported drug allergy, ever conducted. Although this kind of studies bear major limitations that will be discussed below in detail, we think that our study provides important information on risk factors for severe reactions and on the self-perception of drug allergy and subsequent behavior of the sufferers in relation to future consumption of the culprit drugs. The actual prevalence in the general population may be more appropriately addressed through spontaneous reporting to Pharmacovigilance Programs although several factors as the complexity of drug allergies, the patients' perception, the somewhat obscure distinction between true allergic and other hypersensitivity reactions critically influence the reported prevalence.^{6–7} Data from the Italian Interrogational Group of Pharmacovigilance were reviewed specifically for orally administered drugs with 11.6% of the reactions been attributed to drug hypersensitivity while antibiotics and NSAIDs were more commonly implicated.⁸ To date, the only published survey on self-reported drug allergy was conducted among 2309 Portuguese adults and prevalence was estimated to be 7.8%.⁹

Investigation of possible risk factors for drug allergy was a principal concern of this study, as previous epidemiological studies were conducted on specific populations or gave inconclusive results.^{10,11} Risk factors including drug and host related factors; ethnicity and genetics appear to be increasingly important in the predisposition to certain types of drug allergy.¹² From the clinical perspective, female predominance (almost 60%) is in concordance to all previous studies.^{9,13} Other risk factors as atopic status, previous reactions to different pharmacological agents, and chronic illnesses were present in a significant percentage of individuals (31.5, 51.5 and 13.9% respectively). Concerning the relevance of age to the development of drug allergy, a matter not yet fully elucidated¹⁴ our findings are probably biased by the fact that certain age groups are underrepresented on internet surveys. Specific questions concerning concomitant factors that may promote or aggravate reactions were addressed; fever and infection were most common, probably accounting for the antibiotic and/or NSAID

Table 4

Multivariate logistic regression analysis for allergological evaluation.

Variables retained	Category or increment	OR (95% CI)	p-value
Vaccine as the allergenic agent	Vaccines vs. all others	2.54 (1.00–6.46)	0.050
Personal history of another allergy	Yes vs. No	1.76 (1.39–2.24)	<0.001
Treating physician of specialty other than allergology	Treating physician of a specialty other than allergist vs. treated by an allergist	0.07 (0.05–0.09)	<0.001
No physician's consultation	No treating physician vs. treated by an allergist	0.02 (0.01–0.03)	<0.001

OR, odds ratio; 95% CI, confidence interval.

consumption that caused the reaction. Emotional stress was also commonly reported among the reactors.

In all epidemiological studies, skin was the organ most commonly affected by drug hypersensitivity reactions. Among hospitalized patients, skin involvement was observed in the 70–98% of cases, regardless of the type of the hypersensitivity reaction (immediate or delayed).^{15,16} In our population, cutaneous symptoms were also the leading complain, reported by almost half of the participants.

Data on re-exposure are particularly interesting; surprisingly one out of three patients was re-exposed to the offending drug and the majority (75.4%) reacted again in a similar pattern. A recent study evaluating physician knowledge and practice patterns regarding drug allergy in a university medical center revealed that only 30.64% of patients would react if given the suspended drug again but only 15.05% stated that they would give the drug in this situation.¹⁷ According to our findings patients suffering from a chronic disease, those with a history of previous surgeries or those reporting reactions to multiple drug classes were more frequently re-exposed. A probable explanation is that in allergic reactions during multiple drug intakes, the culprit drug may probably elude and not be abolished. Re-exposure without proper testing and consultation by an allergist should be avoided as potentially harmful.¹⁸ A recent study investigating the perception of drug allergy among 800 family doctors from Bucharest, via questionnaire with 21 specific questions either directly or via internet, revealed an underestimation of the severity of drug allergy, a surprisingly high percentage of allergy skin tests or blood tests recommended by general practitioners without specialist advice, and persistent confidence in alternative medicine.¹⁹

Hospitalization is a relatively accurate indicator of more severe adverse reactions to drugs. The multivariate analysis of our survey revealed an increased risk for hospitalization in cases with alarming symptoms (i.e. from the cardiovascular or the lower respiratory systems), prior history of multiple drug allergies and intravenous administration of drugs.

Standard limitations exist in an internet based study and must be considered carefully at the interpretation of the results. The major weakness of the study is the questionnaire-based self-reporting of reactions occasionally reflecting what the participants perceive to be allergic in nature. Objective evaluation of the quality or the severity of symptoms present during these reactions as well as proper diagnostic procedures, even when applied, were not recorded in this survey. Additionally, participants cannot be randomly selected. On the other hand, the number of participants enrolled is considerably high and moreover increasing the strength of the statistical analysis. In conclusion our study presents the real life situation of drug allergy according to patients' perception. The often misguided perception may hamper compliance or future efforts for optimal therapy. Even worse, re-exposure to a drug allergen may cause a devastating allergic reaction. Among others,

Table 3

Multivariate logistic regression analysis for repeated intake of the culprit drug.

Variables retained	Category or increment	OR (95% CI)	p-value
Chronic concomitant disease	Yes vs. no	1.61 (1.25–2.07)	<0.001
Male sex	Male vs. female	1.42 (1.17–1.73)	0.001
Allergy to Non-steroid anti-inflammatory drugs	Non-steroid anti-inflammatory drugs vs. all others	1.40 (1.06–1.85)	0.018
Prior surgery	Yes vs. no	1.38 (1.15–1.67)	0.001
Reactions to drugs of more than one different classes	More than one vs. one drug class	1.36 (1.11–1.65)	0.003
Hospitalization due to drug allergy	Yes vs no	0.75 (0.61–0.90)	0.003
Antibiotics as offending drug	Antibiotics vs. all other medications	0.75 (0.58–0.97)	0.028
Injected administration of the drug at the first episode	Injection (IV, IM, SC) vs. all other ways of administration	0.65 (0.47–0.90)	0.010

OR, odds ratio; 95% CI, confidence interval.

our study dictates the need for better acknowledgement and referring of hypersensitivity reactions to drugs.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.alit.2016.04.016>.

Conflict of interest

The authors have no conflict of interest to declare.

Authors' contributions

MM designed the study, contributed to interpretation of results, have written the manuscript and approved its final submitted version; TNS performed data collection and statistical analysis; XA contributed substantially to the writing of the manuscript; ST contributed substantially to interpretation of results; EP contributed to data collection and interpretation of results; DR substantially revised the manuscript; TP substantially contributed to study planning, statistical analysis, interpretation of results and manuscript writing. All authors read and approved the final manuscript.

References

- Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: report of the nomenclature review committee of the World Allergy Organization, Oct 2003. *J Allergy Clin Immunol* 2004;**113**:832–6.
- Demoly P, Viola M, Gomes ER, Romano A. Epidemiology and Causes of Drug Hypersensitivity. In: Pichler WJ, editor. *Drug Hypersensitivity*. Basel: Karger; 2007. p. 2–17.
- Stephens M, Fox B, Kukulka G, Bellamy J. Medication, allergy and adverse drug event discrepancies in ambulatory care. *Fam Med* 2008;**40**:107–10.
- Kalogeromitros D, Psaltopoulou T, Makris M, Koti I, Chliva C, Stafanadi E, et al. Can internet surveys help us understanding allergic disorders? – results from a large survey in urticaria in Greece. *J Eur Acad Dermatol Venereol* 2011;**25**:532–7.
- Kalogeromitros D, Makris MP, Chliva C, Sergentanis TN, Church MK, Maurer M, et al. An internet survey on self-reported food allergy in Greece: clinical aspects and lack of appropriate medical consultation. *J Eur Acad Dermatol Venereol* 2013;**27**:558–64.
- Bousquet PJ, Demoly P, Romano A, Aberer W, Bircher A, Blanca M, et al. Pharmacovigilance of drug allergy and hypersensitivity using the ENDA-DAHD database and the GALEN platform. The Galenda project. *Allergy* 2009;**64**:194–203.
- Thong BY, Mirakian R, Castells M, Pichler W, Romano A, Bonadonna P, et al. A World Allergy Organization international survey on diagnostic procedures and therapies in drug allergy hypersensitivity. *World Allergy Organ J* 2011;**4**:257–70.
- Demoly P, Adkinson NF, Brockow K, Castells M, Chiriac AM, Greenberger PA, et al. International consensus on drug allergy. *Allergy* 2014;**69**:420–37.
- Salvo F, Polimeni G, Cutroneo PM, Leone R, Conforti A, Moretti U, et al. Allergic reactions to oral drugs: a case/non-case study from an Italian spontaneous reporting database (GIF). *Pharmacol Res* 2008;**58**:202–7.
- Gomes E, Cardoso MF, Praça F, Gomes L, Marino E, Demoly P. Self-reported drug allergy in a general adult Portuguese population. *Clin Exp Allergy* 2004;**34**:1597–601.
- Gomes ER, Demoly P. Epidemiology of hypersensitivity drug reactions. *Curr Opin Allergy Clin Immunol* 2005;**5**:309–16.
- Thong BY, Tan TC. Epidemiology and risk factors for drug allergy. *Br J Clin Pharmacol* 2011;**71**:684–700.
- Barranco P, Lopez-Serrano MC. General and epidemiological aspects of allergic drug reactions. *Clin Exp Allergy* 1998;**28**(Suppl 4):61–2.
- Demoly P, Bousquet J. Epidemiology of drug allergy. *Curr Opin Allergy Clin Immunol* 2001;**1**:305–10.
- Thong BY, Leong KP, Tang CY, Chnq HH. Drug allergy in a general hospital: results of a novel prospective inpatient reporting system. *Ann Allergy Asthma Immunol* 2003;**90**:342–7.
- Park CS, Kim TB, Kim SL, Kim JY, Yang KA, Bae YJ, et al. The use of an electronic medical record system for mandatory reporting of drug hypersensitivity reactions has been shown to improve the management of patients in the university hospital in Korea. *Pharmacoepidemiol Drug Saf* 2008;**17**:919–25.
- Sturm JM, Temprano J. A survey of physician practice and knowledge of drug allergy at a university medical center. *J Allergy Clin Immunol Pract* 2014;**2**:461–4.
- Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin “allergy” in hospitalized patients: a cohort study. *J Allergy Clin Immunol* 2014;**133**:790–6.
- Leru. Drug allergies in primary care practice in Romania: a questionnaire – based survey. *Allergy Asthma Clin Immunol* 2014;**10**:16–8.