Journal of Infection (2015) 70, 237—246

BIAMM
British Infection Association

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Q-fever patients suffer from impaired health status long after the acute phase of the illness: Results from a 24-month cohort study

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Accepted 26 October 2014
Available online 1 November 2014

KEYWORDS
Q-fever;
Coxiella burnetii;
Health status;
Quality of life

Summary *Objectives:* During the largest Q-fever outbreak ever reported, a cohort study was established to assess the health status of Q-fever patients over a 24-month period and to identify factors associated with health status.
Methods: Laboratory-confirmed Q-fever patients participated at six time points after onset of illness. Scores on twelve subdomains from two health status instruments were calculated for each time point to determine progression and compare to reference groups.
Results: The study included 336 Q-fever patients. There is a significant linear improvement over time in nine of the twelve health status subdomains. For example, the proportion of patients with severe fatigue improved from 73.0% at three months to 60.0% at twelve months and 37.0% at twenty-four months, but this was still high compared to a healthy reference group (2.5%). For the three most severely affected subdomains -'Fatigue', 'General Quality of Life'

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http://dx.doi.org/10.1016/j.jinf.2014.10.010

and 'Role Physical'- the baseline characteristics significantly associated with a long-term reduced health status were being female, being a young adult and having pre-existing health problems.
Conclusions: Despite a significant linear improvement over time in nine of the twelve health status subdomains, more than one out of three patients still suffered from a reduced health status at 24 months.

Introduction

Q-fever is a zoonosis caused by the intracellular bacterium *Coxiella burnetii*. Approximately 40% of all persons infected with Q-fever develop symptoms such as fever, pneumonia and hepatitis.[1,2] Several studies have shown that many patients suffer from a severely impaired health status, including persistent fatigue, after Q-fever.[3–9] These symptoms have been reported for as long as ten years after onset of illness,[5] but there are no data on how symptoms evolve over time during the first two years after infection.

Q-fever is known to occur in small local outbreaks in Western Europe (.19 cases per 100,000 in 2011 in Europe, ranging from .00 in nine EU countries to .60 per 100,000 in Cyprus[10]), which are usually associated with livestock farming.[1,11] Between 2007 and 2009, the number of notified cases of Q-fever increased annually in the Netherlands, a country of 17 million inhabitants, and reached a cumulative total of 4107 in 2011, making it the largest documented outbreak in the world.[12] Measures taken in late 2009 to prevent the further spread of the disease led to a massive reduction in notifications from 2010 onwards (there were 81 cases in 2011).[12]

A study carried out in the Netherlands in 2009 found that there were high levels of severe fatigue and low levels of general quality of life 12–26 months after infection.[8] In addition, the Dutch Q-fever patient organisation reported many long-term impairments (e.g. severe symptoms of fatigue, depression and unemployment).[13] In order to provide prospective data on Q-fever patients, we established a cohort study to systematically asses health status progression over a 24-month period. We also identified individual characteristics associated with health status at 12 and 24 months.

Materials and methods

The design used was a prospective cohort study of Q-fever patients over a period of 24 months after onset of illness. The study protocol was submitted to the Medical Ethical Review Board of the region Arnhem-Nijmegen, which indicated that ethical review was not required.

The study population was patients diagnosed with Q-fever in 2010 and 2011 in the Netherlands, who were at least 18 years of age and fulfilled the Dutch notification criteria of Q-fever.[14] The standard treatment for patients with a Q-fever infection used by general practitioners in the Netherlands is 2–3 weeks of antibiotics, preferably Doxycycline (200 mg per day).[12]

Data collection

All Municipal Health Services in the Netherlands were asked to invite Q-fever patients who met the Dutch notification criteria to participate in the study. Patients who gave permission received an information letter and a consent form by postal mail. After receiving written consent, patients were contacted by postal mail at 3, 6, 9, 12, 18 and 24 months with a questionnaire, and patients who did not return the questionnaire received a reminder by telephone or postal mail. Patients were allowed to enter the study at 3, 6, 9 or 12 months after onset of illness.

Questionnaire

The study questionnaires contained two instruments to measure health status and quality of life: the Nijmegen Clinical Screening Instrument (NCSI)[15] and the Short Form 36 (SF-36).[16] The NCSI was originally developed to measure health status in COPD patients and provides normative data indicating normal functioning, mild or severe problems for each subdomain.[15] The NCSI and SF-36 were used simultaneously since they gather information on different domains. Only the four subdomains in the SF-36 that have been shown to be not conceptually similar to subdomains in the NCSI are presented in our study.[17] The NCSI was included at 3, 12, 18 and 24 months.

Information on the individual characteristics of Q-fever patients that could affect health status was also collected at the time of inclusion and consisted of socio-demographic, lifestyle and medical aspects (self-reported). Characteristics which could change over time (e.g. smoking behaviour and BMI) were included in successive questionnaires.

Reference groups

To compare the NCSI scores of the Q-fever patients, an existing reference group, consisting of healthy participants,[15] was expanded to match our group of Q-fever patients for age and gender. They were asked to visit Radboud university medical center, where they completed an electronic questionnaire, including the NCSI. The lung function of the healthy reference group was tested, so that persons with an undiagnosed underlying respiratory illness that could affect their health status could be excluded. For the SF-36 scores, we compared our scores to a large general population study carried out in the US.[18]