aHUS Global Poll 2014- A Commentary on the Data

Introduction

atypical Haemolytic Uraemic Syndrome is a genetic, progressive, life-threatening disease mostly resulting from chronic, uncontrolled complement activation. It is characterized by systemic thrombotic microangiopathy (TMA), clotting and red blood cell destruction leading to renal and other organ end damage.

The aHUS Global Poll came about as a result of a discussion by the aHUS Community within the Rare Connect communication platform of EURORDIS. International aHUS Patient Organisations from Spain, UK, USA and Canada agreed to support a 2014 survey of aHUS patients from as many countries as could be reached out to.

A questionnaire was drafted by a small working group of representatives from aHUS patient organisations and EURORDIS. Questions were designed to address the key rare disease themes of diagnosis, treatment and commissioning, research and registries, societal impact and access to a centre of excellence and information; as well as finding out some key characteristics of those being surveyed.

To make the survey as inclusive as possible ,the questionnaire was translated into French Spanish German Italian and Dutch versions, transferred to a Survey-Monkey format and then posted on the Rare Connect website from Mid February to early April 2014.By the time the survey was closed 214 responses had been received from 17 countries (see Annex A) (Q4). 107 responses were given by aHUS patients themselves and the same number of Parents/Carers responded on behalf of their family member (Q1).

Characteristics of patients included in the survey

Of the 214 aHUS patients included in the Survey almost two thirds (64%) were reported as being female with just 36% being male (Q2). There appeared to be no gender difference in respondents up to 18 years (41 to 41) but it is in the adult group that females vastly outnumber males (95 to 37). Only in the preteens group do boys slightly outnumber girls (36 to 32). Children up to 10 years of age were the largest reported group (28%) and the next largest group (21%) were aged 30 to 40 years (Q3). The average age of all respondents was 27 years.

The majority of patients (54%) reported that they had their first severe episode of aHUS before their 21st birthday and for most of those it was even before they were 10 years old. Very few became ill (4%) after their 50th birthday so most of the remaining patients became ill in early adult hood to middle age (Q5). The average time respondents have been living with the illness is 8 years, making 19, the average age of onset.

Of the respondents who had been given the results of their genetic test around 25% (53) had no identifiable genetic predisposing factor for aHUS. Nearly three quarters (89) of those who tested positive had a Complement Factor H mutation, with or without a related CHFR mutation, or anti-factor H antibodies, the latter being much higher than was expected. Of the

remainder 14 had C3, 9 had CD46/MCP, 5 with CFI, 5 and 3 with CFB. There were no respondents with the recently identified mutation DGKE. (Q7)

Diagnosis

Remarkably for a rare disease where a diagnosis is hard to get, 84% of respondents reported that they had been diagnosed with aHUS within one year of becoming ill, and half of them claimed they were given their diagnosis within a week. A significant number of long term patients, whose first or earlier encounter many years ago (up to 25 years ago in one case) went unexplained only to be led to a correct diagnosis from a more recent episode. (Q12).

Oddly only a third of patients reported that they were initially diagnosed with typical HUS/TTP and a similar number confirmed that they were tested for Shigatoxin/e coli and ADAMTS15 deficiency, when it would have been thought likely that such tests would be routinely given to rule out those as a cause of their TMA. (Q10/11).

Less than 1 in 8 aHUS patients had not had access to genetic screening, but for those with a rare disease a very high number of aHUS patients (77%) have had access to genetic screening and knew their result, or were waiting for the results (6%). (Q6)

Nearly half of patients (48%) received the results of their genetic tests within three months; but there is some room for improvement in the time taken as over a third of patients had to wait six months to more than a year; and particularly as 2 patients reported that they were given the results of their tests within a week. (Q8)

More patients (114) reported that they had no experience of any unexplained clinical symptoms before their catastrophic encounter with aHUS, than had. But of those who had a significant number reported that they had one or more of the early clinical symptoms listed, with most having asthma like breathing problems or allergy like swellings of face or arms/legs, and skin lesions or “hives”. A higher number of patients (16) than would have been thought had experienced discolourisation to the tips of their fingers. Of those who reported “other” clinical symptoms, frequent headaches and backache were mentioned most. Whilst many of these symptoms are mild and common and would not prompt consideration of aHUS for most people, for those genetically predisposed or related to someone with aHUS ,they could be an indication worthy of further exploration.(Q15)

Just less than half of patients reported that they did not know what could have triggered their aHUS, but of the majority who believed they did, most reported that they thought a viral or bacterial infection preceded it, with a smaller group reporting a possible link with pregnancy, giving birth or birth control. A smaller number reported that they had been vaccinated (e.g. for Swine Flu) just before they became ill with aHUS. (Q9)

Nearly two thirds of patients received an accurate diagnosis by just visiting two doctors, which is surprising for a rare disease, but 25 % of patients experienced the more typical rare disease experience of visiting 5 or more doctors before a diagnosis was obtained. (Q13)

The early diagnosis could be explained because those presenting with the acute kidney injury caused by aHUS would be quickly referred to a nephrologist (191 patients) together with either a haematologist (90) or a paediatrician (60). (Q14)

Around 25% of respondents reported one or more of the consequences of an earlier misdiagnosis, with physical and psychological affects and a loss of confidence in the medical professional cited as the worst of outcomes. But 155 patients reported that they had not experienced misdiagnosis, or, even if they did, any lasting adverse outcome. (Q16)

Treatment & Commissioning

Just under half (48%) of respondents were receiving eculizumab to treat their aHUS and another 15% were receiving eculizumab to support a kidney transplant. A small number (7%) were being treated by Plasma Exchange. A significant number (30%) of patients regarded themselves as not requiring any treatment for aHUS at present. (Q 18)

Given the high level of patients surveyed who were receiving eculizumab it followed that most respondents (69%) did not need renal replacement therapy, and ,of those who did, just over a quarter (27%) were receiving either peritoneal(5%) or haemolytic dialysis(22%). There was a small minority (4%) who have a working kidney transplant without eculizumab support. (Q19).

Almost three quarters of patients responding agreed that they were receiving the treatment they would chose. 16% said they definitely were not and just 10% were unsure. (Q20)

Commissioning of aHUS treatment depended largely on the way in which health service was funded in each country. Of those receiving eculizumab, less than half had it commissioned by either their country's health service (41%) or reimbursed by their social security office (7%). Private health insurance covered the cost for 20% of patients and a small number (13%) were getting it supplied on compassionate grounds or by another charitable means (following a trial). In 16% of responses, patients were unsure how it was paid for. (Q21)

Whilst the majority of patients (54%) reported that they had access to a National Expert Centres and some cited locations where internationally recognised aHUS clinicians practiced e.g. Newcastle upon Tyne, Iowa, Bergamo, most respondents regarded their local hospitals as centres of excellence. (Q17)

Research and Registries

Only about 1 patient in 3 knew that they had participated in research i.e. about 70 patients. The majority said they had not, and there were a small number who said they were unsure. So there is scope for including more patients into aHUS research if they were prepared to do so. (Q23)

As far as being prepared to do so however 6 patients (3%) said would not be prepared to be part of aHUS research, but 80 % said they definitely would with another 17% wanting to

consider it a bit more before deciding. Having 80% of the global aHUS population available for research would be beyond many aHUS researchers' expectations; but it is possible that it could be more than that if some of the "don't knows" receive the information they need to make a decision.(Q24)

Less than half of patients said they definitely were in an aHUS Registry. About 50 said they were not and an amazing 65 or so patients said they did not know. This response says something about the environment in which patients find them themselves when it comes to research. They may want to participate but cannot do so because responsibility for enrolling them and informing them about research registries rests with their clinicians. (Q25)

Societal Impact

People with rare diseases frequently encounter major life style changes but most aHUS patients said that was not their experience. But by far the biggest effect on those whose treatment burden did impact was a significant loss of education and employment time. A sizeable number of responses reported strains on and breakdown of family relationships demonstrating how a serious and chronic illness impacts beyond the patient. (Q22)

Access to information

Very few patients reported that they had no access to information about their illness. aHUS Specific Websites and their hospital's Clinicians stand out as the key source of information, but the internet generally provided data, either from medical publications, or, to a lesser extent from renal and rare disease organisations. (Q26)

The aHUS specific organisations were well known beyond their membership with the Foundation for children with atypical HUS having the highest international recognition followed by Rare Connect and aHUSUK in almost equal measure. But generally all aHUS patient organisation had achieved a high penetration of awareness amongst the patients responding from their specific countries. This is commendable as such aHUS organisations have only existed for just a few years. (Q27/28)

Concluding comment

This is the first occasion in which the Global aHUS Patient Community has joined together to produce information about itself, collectively; to help improve awareness and understanding of aHUS. The published statistics, and resulting EURORDIS info graphs, will continue to, not only provide insights to those new to living with aHUS, but also provide topics for further discussion and action within the aHUS Community.