2.3 Invasive Group A Streptococcal Disease

Summary

Total number of cases, 2015 = 107

Crude incidence rate, 2015 = 2.3 per 100,000 population

Notifications

In 2015, 107 cases of invasive group A streptococcal (iGAS) disease were notified, which was the lowest figure in four years. This corresponds with a rate of 2.33 iGAS cases per 100,000 population [95% confidence interval (CI): 1.91-2.82], lower than that seen in 2014 (3.57 [95% CI: 3.13 – 4.26]). This decrease is statistically significant.

Case classification

The majority were classified as confirmed cases (n=105; 98%): patients with group A streptococcus (GAS; *Streptococcus pyogenes*) isolated from a sterile site. Two were classified as probable iGAS cases: patients with streptococcal toxic shock syndrome (STSS) or necrotising fasciitis and GAS isolated from a non-sterile site (e.g. throat, sputum, leg wound).

Patient demographics

Of the 107 cases, 60 (56%) were male. The mean age was 43 years (range = 5 months – 99 years) and iGAS was more common in young children and older adults (Figure 1).

Geographic spread and seasonal variation

Table 1 displays the numbers and crude incidence rates (CIRs) of iGAS disease by HSE area from 2011 to 2015. While HSE East accounted for the highest number of reported cases in 2015 (n=40), HSE West had the highest CIR (3.82 per 100,000 population). In two HSE areas, Midlands and Northwest, both the numbers of cases and CIRs increased, while in the other six HSE areas, decreases were reported.

The peak month in 2015 was July (15 cases), followed by April, June and December (12 cases each). Contrary to previous years, there were more cases reported in the second half (July – December: 61 cases) than the first half of the year (January – June: 46 cases) (Figure 2). Figure 3 displays cumulative monthly iGAS cases from 2011 to 2015 inclusive. An increase in notifications which occurred from April 2012 was sustained throughout 2013 and into 2014, with a stabilisation in the latter months of 2014. The opposite can be said of 2015, where the number of cases was much lower than normal in the earlier months, increasing towards the end of the year. Data presented are based on the date the case was notified to Public Health, not on the date the case was first detected.

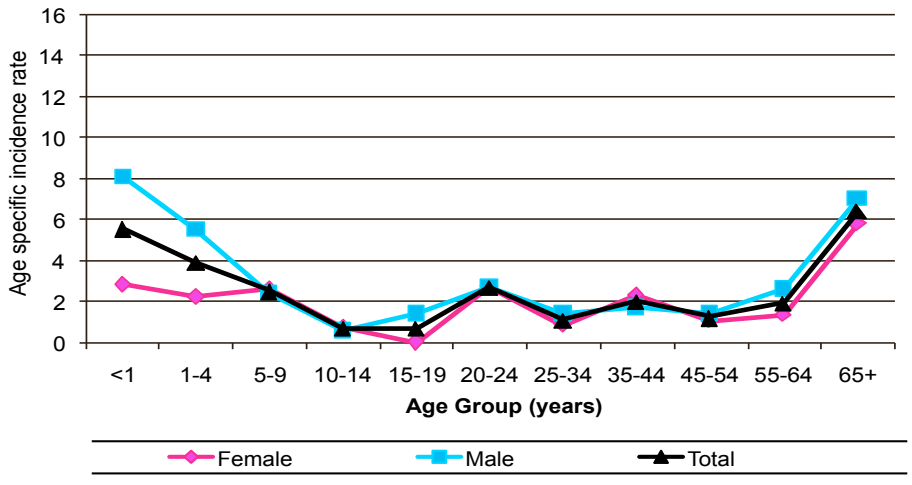

Figure 1. Age and sex specific rates of iGAS disease in 2015

Isolate details

Of 105 confirmed cases, GAS was isolated from a sterile site in 79, with source site not reported for 26. Of reported sterile sites, GAS was isolated primarily from blood cultures (n=57; 72%), deep tissue (n=9; 11%), joints (n=5; 6%), abscesses (n=4; 5%), pleural fluid (n=1; 1%), bone (n=1; 1%), drain fluid (n=1; 1%) and cerebrospinal fluid (CSF) (n=1; 1%). For two cases, GAS was isolated from another sterile site in addition to blood: tissue (n=1) and joint (n=1).

Of the two probable cases, GAS was isolated from non-sterile sites (superficial wound swabs). There were no possible cases of iGAS notified.

Typing data, based on sequencing of the *emm* genes that encode the M protein (the major virulence factor), were available on 92 isolates submitted from 27 laboratories: *emm*-types 1 (n=27; 29%), 12 (n=14; 15%), 28 (n=12; 13%), 89 (n=8; 9%), 3 and 4 (n=4; 4% each) comprised 74% of all the isolates typed. Fifteen other *emm*-types (each represented by ≤3 isolates) were also detected. Of the 10 patients with STSS for whom *emm*-typing was undertaken, four GAS isolates belonged to *emm*1 (40%) and three to *emm*12 (30%).

Enhanced surveillance data

Enhanced data were provided for 96 (90%) of 107 iGAS cases. The source laboratory could be ascertained for all cases. As in previous years, there was wide variation in completeness of enhanced data reporting. Table 2 summarises characteristics of iGAS cases in Ireland from 2011 to 2015.

Clinical details

Clinical presentation data were provided for 89 cases (83%). As in previous years, bacteraemia (n=64 cases, including cases where bacteraemia was not specifically stated but GAS was isolated from blood) and cellulitis (n=34) were the commonest presentations, followed by septic arthritis (n=13), pneumonia (n=12), STSS (n=11; two of which were implied based on the information provided on the clinical presentation), puerperal sepsis (n=6), necrotising fasciitis (n=5), meningitis (n=4), peritonitis (n=3), myositis (n=2) and erysipelas (n=1). Note that an iGAS case could have more than one clinical manifestation of infection.

Risk factors

Risk factor data were provided for 77 iGAS cases (72%). Risk factors included: presence of skin or wound lesions (n=32), diabetes mellitus (n=7), malignancy (n=6), steroid use (n=6),

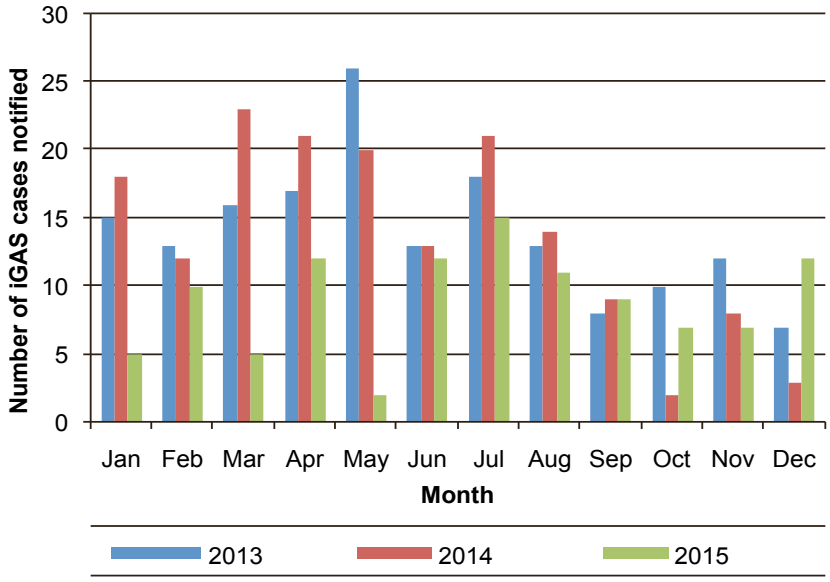

Figure 2. Monthly distribution of iGAS cases, 2013-2015

Table 1. Numbers (n) and Crude Incidence Rates (CIRs) per 100,000 population of iGAS disease by HSE Area (2011-2015)

HSE Area	2011		2012		2013		2014		2015	
	n	CIR	n	CIR	n	CIR	n	CIR	n	CIR
HSE E	29	1.79	51	3.15	67	4.14	65	4.01	40	2.47
HSE M	5	1.77	7	2.48	7	2.48	4	1.42	7	2.48
HSE MW	6	1.58	8	2.11	16	4.22	13	3.43	6	1.58
HSE NE	1	0.23	11	2.50	14	3.18	12	2.72	10	2.27
HSE NW	2	0.77	5	1.94	6	2.32	3	1.16	7	2.71
HSE SE	7	1.41	16	3.22	21	4.22	18	3.62	9	1.81
HSE S	12	1.81	14	2.11	18	2.71	27	4.06	11	1.66
HSE W	5	1.12	10	2.25	19	4.27	22	4.94	17	3.82
IRELAND	67	1.46	122	2.66	168	3.66	164	3.57	107	2.33

CIRs calculated using the 2011 census

recent childbirth (n=5), varicella infection (n=3), alcoholism (n=3), injecting drug use (IDU) (n=3) and non-steroidal anti-inflammatory drug (NSAID) use (n=1). Note that an iGAS case could have more than one risk factor. No risk factors were identified for 24 cases.

Clinical management/severity
Surgical intervention was required for 26 patients (age range = 2 months – 85 years). This included four patients with STSS and three patients with necrotising fasciitis.

Among patients requiring surgical intervention, risk factor data were provided for 20 cases. Risk factors included: skin and wound lesions (n=12), age ≥65 years (n=3), malignancy (n=1), IDU (n=1) and NSAID use (n=1). Note that an iGAS case requiring surgery could have more than one risk factor. No risk factors were identified for six patients.

Twenty-five patients (aged 12 months – 84 years) required intensive care unit (ICU) admission. This included nine patients with STSS and three patients with necrotising fasciitis.

Among patients admitted to an ICU, risk factor data were provided for 22. Risk factors included: age ≥65 years (n=9), skin and wound lesions (n=9), diabetes mellitus (n=3), alcoholism (n=2), IDU (n=1) and varicella infection (n=1). Note that an iGAS case requiring ICU admission could have more than one risk factor. No risk factors were identified for seven patients. Length of ICU stay was provided for 12 cases. The median length of ICU stay was three days (range = 1 – 18).

Other epidemiological information
Seven cases of iGAS were reported as hospital-acquired in 2015.

There was one iGAS outbreak reported in 2015. This was a family outbreak in HSE-E, with three people reported ill. However, just one of the three cases was a confirmed invasive infection. There were also two outbreaks of scarlet fever reported in 2015; one in a crèche with four reported ill and the other in a school with two reported ill.

Outcome
Outcome at seven days following GAS detection was reported for 73 cases:

- 66 were still alive
- Six patients had died, where GAS was the main or contributory cause of death

The seven-day case fatality rate (CFR) for iGAS disease was 9.5%.

Of 11 STSS cases, outcome at seven days was reported for seven. Of those, there was one death due to GAS (CFR = 14%).

Of 26 cases requiring surgical intervention, outcome at seven days was reported for 19. Of those, there were no deaths due to GAS.

Of 25 cases admitted to ICU, outcome at seven days was reported for 17. Of those, there was one death due to GAS (CFR = 6%).

Antimicrobial susceptibility
Antimicrobial susceptibility data were reported on 79 GAS isolates (63 from blood and 16 from other specimens) by 23 laboratories via the European Antimicrobial Resistance Surveillance Network (EARS-Net). All isolates tested were susceptible to penicillin (n=75) and vancomycin (n=56). Resistance to erythromycin was reported in five (7%) of 70

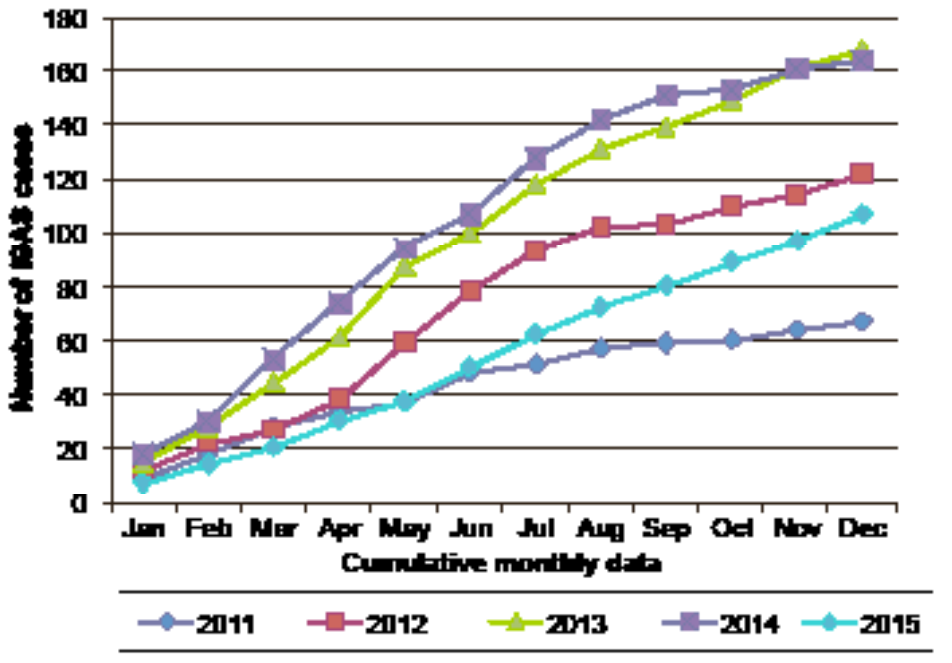

Figure 3. Cumulative monthly numbers of iGAS cases, 2011-2015

Table 2. Characteristics of iGAS cases in Ireland, 2011-2015

	2011	2012	2013	2014	2015
Notifications					
Total iGAS cases notified	67	122	168	164	107
iGAS incidence rate per 100,000 population	1.46	2.66	3.66	3.57	2.30
Cases for which Enhanced data provided** (%)	60 (90%)	106 (87%)	156 (93%)	150 (91%)	96 (90%)
Patient Demographics					
Male (%)	28 (42%)	59 (48%)	95 (57%)	94 (57%)	60 (56%)
M:F ratio	0.72:1	0.94:1	1.30:1	1.34:1	1.19:1
Mean age	43	44	41	44	43
Median age	39	42	40	44	42
Age range	0-97	0-92	0-93	0-99	0-99
Paediatric cases (aged <18 years) (%)	15 (22%)	28 (23%)	45 (27%)	47 (29%)	26 (24%)
Older cases (aged 65+ years) (%)	22 (33%)	42 (34%)	50 (30%)	56 (34%)	34 (31%)
Clinical Presentation†					
Data on Clinical Presentation (%)	58 (87%)	103 (84%)	142 (85%)	132 (80%)	89 (83%)
Streptococcal Toxic Shock-like Syndrome (STSS) without NF (%)	4 (7%)	22 (21%)	28 (20%)	18 (14%)	11(12%)
Necrotising fasciitis (NF) without STSS (%)	1 (2%)	2 (2%)	6 (4%)	4 (3%)	5 (6%)
STSS and NF (%)	2 (3%)	4 (4%)	4 (3%)	3 (2%)	0 (0%)
Bacteraemia with focal presentations (%)	30 (52%)	42 (41%)	45 (32%)	43 (33%)	34 (38%)
Bacteraemia with no focal presentations (%)	15 (26%)	21 (20%)	36 (25%)	34 (26%)	22 (25%)
Other focal presentations with no bacteraemia (%)	6 (10%)	11 (11%)	23 (16%)	30 (23%)	17 (19%)
Bacteraemia (%)	52 (90%)	80 (78%)	107 (75%)	95 (72%)	64 (72%)
Other focal presentations:					
Cellulitis (%)	24 (41%)	41 (40%)	45 (32%)	58 (44%)	34 (38%)
STSS (%)	6 (10%)	26 (25%)	32 (23%)	21 (16%)	11 (12%)
Pneumonia (%)	8 (14%)	17 (17%)	24 (17%)	14 (11%)	12 (13%)
Septic arthritis (%)	2 (3%)	7 (7%)	10 (7%)	11 (8%)	13 (15%)
Necrotising fasciitis (%)	3 (5%)	6 (6%)	10 (7%)	7 (5%)	5 (6%)
Myositis (%)	0 (0%)	4 (4%)	3 (2%)	6 (5%)	2 (2%)
Puerperal sepsis (%)	5 (9%)	6 (6%)	6 (4%)	4 (3%)	6 (7%)
Erysipelas (%)	0 (0%)	3 (3%)	3 (2%)	2 (2%)	1 (1%)
Peritonitis (%)	3 (5%)	1 (1%)	4 (3%)	1 (1%)	3 (3%)
Meninigtis (%)	1 (2%)	3 (3%)	3 (2%)	0 (0%)	4 (4%)
Risk Factors†					
Data on Risk Factors (%)	49 (73%)	96 (79%)	138 (82%)	126 (77%)	77 (72%)
Skin lesions/wounds (%)	20 (41%)	34 (35%)	56 (41%)	50 (40%)	32 (42%)
Diabetes (%)	7 (14%)	5 (5%)	16 (12%)	11 (9%)	7 (9%)
Malignancy (%)	6 (12%)	10 (10%)	23 (17%)	10 (8%)	6 (8%)
Varicella (%)	2 (4%)	9 (9%)	5 (4%)	7 (6%)	3 (4%)
Steroid use (%)	1 (2%)	8 (8%)	11 (8%)	6 (5%)	6 (8%)
Alcoholism (%)	1 (2%)	5 (5%)	6 (4%)	5 (4%)	3 (4%)
Injecting drug user (%)	3 (6%)	6 (6%)	5 (4%)	5 (4%)	3 (4%)
Childbirth (%)	5 (10%)	6 (6%)	6 (4%)	4 (3%)	5 (6%)
Non-steroid anti-inflammatory drug use (%)	1 (2%)	2 (2%)	4 (3%)	2 (2%)	1 (1%)
No identified risk factor (%)	12 (24%)	24 (25%)	47 (34%)	47 (37%)	24 (31%)
Outcome at 7 days					
Data on outcome at 7 days (%)	43 (64%)	65 (53%)	108 (64%)	102 (62%)	73 (68%)
RIP/GAS main cause or contributory (%)	5 (12%)	8 (12%)	16 (15%)	10 (10%)	6 (8%)
STSS cases: Data on outcome at 7 days (%)	5 (83%)	17 (65%)	26 (81%)	17 (81%)	7 (64%)
STSS cases: RIP/GAS main cause or contributory (%)	1 (20%)	6 (35%)	10 (38%)	6 (35%)	1 (14%)
Severity					
Data on Admission to ITU (%)	57 (85%)	99 (81%)	153 (91%)	144 (88%)	92 (86%)
Admitted to ITU (%)	11 (19%)	40 (40%)	44 (29%)	36 (25%)	25 (27%)
Data on Surgical Intervention (%)	45 (67%)	86 (70%)	136 (81%)	127 (77%)	86 (80%)
Surgical Intervention Required (%)	8 (18%)	26 (30%)	39 (29%)	41 (32%)	26 (30%)
Typing					
iGAS isolates that were typed (%)		109 (89%)	140 (83%)	130 (79%)	92 (86%)
Emm-1 (%)		53 (49%)	41 (29%)	21 (16%)	27 (29%)
Emm-3 (%)		4 (4%)	33 (24%)	47 (36%)	4 (4%)
Emm-12 (%)		11 (10%)	4 (3%)	6 (5%)	14 (15%)
Emm-28 (%)		8 (7%)	8 (6%)	12 (9%)	12 (13%)
Emm-89 (%)		4 (4%)	13 (9%)	8 (6%)	8 (9%)
Other emm-types (%)		29 (27%)	41 (29%)	36 (28%)	27 (29%)

** Degree of completion of enhanced surveillance forms varies from case to case: information may not be available on all variables/categories, thus calculations of percentages take into account only those cases for which data are provided

†Note: A patient may have more than one clinical presentation or risk factor

isolates, to clindamycin in four (6%) of 65 isolates and to tetracycline in six (12%) of 49 isolates.

CONCLUSION

In 2015, 107 cases of iGAS infection were notified in Ireland, a substantial decrease from that of the previous two years (2014; n=164, 2013; n=168). The CIR decreased from 3.57 in 2014 to 2.3 per 100,000 in 2015 and this was statistically significant.

Invasive GAS is a potentially life-threatening disease. In 2015, the CFR was 9.5% for all iGAS infections and even higher for patients presenting with STSS (14%). For the first time since 2012, there has been a drop in the number of patients presenting with STSS: 2012 (n=26), 2013 (n=32), 2014 (n=21) and 2015 (n=11).

Typing of *emm* genes was undertaken on a national basis for the first time in 2012, with the establishment of a GAS typing service by the Epidemiology and Molecular Biology Unit (EMBU) at the Children's University Hospital, Temple St. In 2015, one *emm* type, *emm*1, predominated comprising 29% of all isolates typed. This is similar to the situation in 2012 when *emm*1 was also predominant comprising 49% of all isolates typed; while in 2013 both emm1 and emm3 were the dominant *emm* types and in 2014, emm3 was the predominant *emm* type, comprising 36% of all isolates typed. Certain *emm* types, including *emm*1 and *emm*3, are associated with STSS and STSS in turn is strongly associated with increased mortality. The changes observed in the predominant *emm* types in circulation and in the clinical presentations over the last couple of years highlight the dynamic nature of iGAS infection.

Ongoing surveillance is essential, specifically completion of the enhanced data questionnaire, to gain a greater understanding of iGAS, to enable early detection of clusters/outbreaks, to ensure prompt implementation of infection prevention and control precautions and appropriate management of contacts. Epidemiological typing as provided by the EMBU is another vital element to increase insight into GAS infection in Ireland, as certain *emm* types are associated with greater morbidity and mortality.

Antimicrobial susceptibility data confirm that iGAS remains susceptible to penicillin and that penicillin should continue to be the treatment of choice for iGAS.

HPSC thanks participating microbiology laboratories and public health departments for their ongoing contribution to the iGAS enhanced surveillance scheme.

All microbiology laboratories are encouraged:

- to return enhanced iGAS surveillance forms for every patient with iGAS
- to submit all iGAS isolates to the Epidemiology and Molecular Biology Unit (EMBU), Children's University Hospital, Temple St for *emm*-typing
- to submit antimicrobial susceptibility data on all iGAS cases along with EARS-Net quarterly returns

Further information on iGAS disease in Ireland, including the enhanced surveillance form, factsheets for patients and contacts and national guidelines is available at: http://www.hpsc.ie/A-Z/Other/GroupAStreptococcalDiseaseGAS/

The figures presented in this summary are based on data extracted from the Computerised Infectious Diseases Reporting (CIDR) System on **22nd July 2016.**