2.3 Invasive Group A Streptococcal Disease

Summary

Number of cases = 148
Crude incidence rate (CIR) = 3.11 per 100,000 population

The figures presented in this summary are based on data extracted from the Computerised Infectious Disease Reporting (CIDR) System on **10th August 2017.**

Notifications

In 2016, both the number and rate per 100,000 population of invasive group A streptococcal (iGAS) infection increased in comparison with 2015. n=148; rate = 3.11 [95% confidence interval (CI): 2.63-3.65] versus n=107; rate = 2.25 [95% CI: 1.84 – 2.72].

Case classification

The vast majority of cases were confirmed iGAS (n=147; 99%), with one probable case (n=1; 1%). A confirmed case has GAS or *Streptococcus pyogenes* isolated from a sterile site. A probable case has a diagnosis of streptococcal toxic shock syndrome (STSS) or necrotising fasciitis and GAS isolated from a non-sterile site.

Patient demographics

Of the 148 cases, 77 (52%) were male. The mean age was 44 years (range = 9 months – 92 years) and iGAS was more common in young children and older adults (Figure 1).

Geographic location and seasonal variation

Table 1 displays annual numbers and crude incidence rates (CIRs) of iGAS by HSE region (2012 – 2016). The highest number of cases and CIR in 2016 were from HSE East (n=68; CIR = 3.97 per 100,000 population). In six other HSE regions, increased iGAS notifications were observed. In HSE Midwest and HSE West, both cases and CIRs decreased in 2016. The peak month in 2016 was March (25 cases), followed by June (16 cases), January and December (14 cases each) (Figure 2). Figure 3 displays cumulative monthly iGAS cases from 2012 to 2016 inclusive. Following a dip in iGAS notifications in early 2015, the numbers subsequently increased in late 2015 and this increase was sustained in 2016. Data presented are based on the date the case was notified to public health, not on the date the case was first detected.

Isolate details

Of 147 confirmed cases, GAS was isolated from a sterile site in 110, with source site not reported for 37. Of reported sterile sites, GAS was isolated primarily from blood cultures

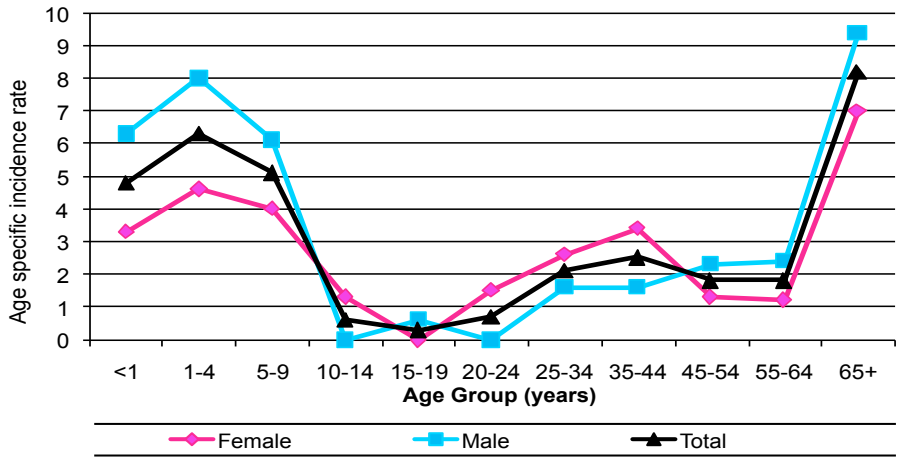

Figure 1. Age and sex specific rates of iGAS infection (2016)

(n=85; 77%), abscesses (n=9; 8%), deep tissue (n=8; 7%), joints (n=6; 5%), pleural fluid (n=1; 1%). For two cases, GAS was isolated from a second sterile site in addition to blood: pleural and pericardial aspirates (n=1) and joint (n=1).

There was one probable case in 2016 where GAS was isolated from a non-sterile site (eye swab). The case presented with orbital cellulitis, which represents a severe GAS infection but is not an iGAS case according to the case definition.

Typing data, based on sequencing of the *emm* genes that encode the M protein (the major virulence factor), were available on 127 isolates submitted from 26 laboratories: *emm*-types 1 (n=51; 40%), 12 (n=14; 11%), 28 (n=10; 8%), 3, 4 and 89 (n=6; 5% each) comprised 73% of all the isolates typed. Fifteen other *emm*-types (each represented by five isolates or less) were also detected. Of the 23 patients with STSS for whom *emm*-typing was undertaken, nine GAS isolates belonged to *emm*1 (39%) and four each to *emm*3 and *emm*28 (17%).

Enhanced surveillance data

Enhanced data were provided for 120 iGAS cases (81%), with variation in completeness of data supplied. Table 2 summarises characteristics of iGAS cases in Ireland from 2012 to 2016.

Clinical details

Clinical details were provided for 111 cases (75%). An iGAS case could have more than one clinical manifestation of infection. As in previous years, bloodstream infection (BSI) (n=90) and cellulitis (n=50) were the commonest presentations, followed by STSS (n=25), pneumonia (n=9), necrotising fasciitis (n=8), septic arthritis (n=7), peritonitis (n=5), erysipelas (n=2), myositis (n=2) and puerperal sepsis (n=2).

Risk factors

Risk factors were described for 93 iGAS cases (62%). An iGAS case could have more than one risk factor. No risk factors were identified for 27 cases.

Reported risk factors included; presence of skin or wound lesions (n=38), diabetes mellitus (n=10), malignancy (n=16), steroid use (n=8), varicella infection (n=8), injecting drug use (IDU) (n=4), alcoholism (n=2), recent childbirth (n=3) and non-steroidal anti-inflammatory drug (NSAID) use (n=2).

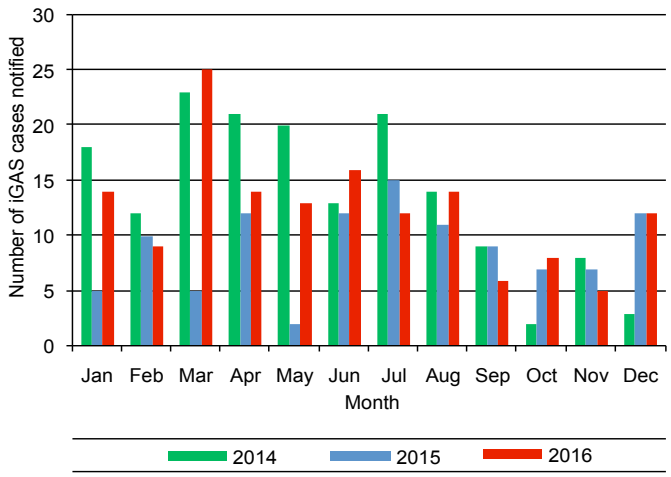

Figure 2. Monthly distribution of iGAS cases, 2014-2016

Table 1. Annual iGAS cases and crude incidence rates (CIRs) per 100,000 population by HSE area (2012-2016).

HSE Area	2012		2013		2014		2015		2016	
	n	CIR	n	CIR	n	CIR	n	CIR	n	CIR
HSE E	51	3.15	67	4.14	65	3.80	40	2.34	68	3.97
HSE M	7	2.48	7	2.48	4	1.37	7	2.39	10	3.42
HSE MW	8	2.11	16	4.22	13	3.39	6	1.56	12	3.13
HSE NE	11	2.50	14	3.18	12	2.60	10	2.17	15	3.25
HSE NW	5	1.94	6	2.32	3	1.17	7	2.73	3	1.17
HSE SE	16	3.22	21	4.22	18	2.61	9	1.30	15	2.17
HSE S	14	2.11	18	2.71	27	5.28	11	2.15	12	2.35
HSE W	10	2.25	19	4.27	22	4.86	17	3.75	13	2.87
IRELAND	122	2.66	168	3.66	164	3.44	107	2.25	148	3.11

CIRs for 2012-2013 were calculated using the 2011 census and for 2014-2016 using the 2016 census

Clinical management/severity

Surgical intervention was required for 28 patients (19%), with an age range = 11 months – 81 years. Of those, four were notified as STSS, five as necrotising fasciitis and two as having both STSS and necrotising fasciitis. Risk factor data on 23 of the surgical cases (82%) was described, with skin and wound lesions (n=10), age ≥65 years (n=6), diabetes (n=2), NSAID use (n=2), varicella (n=2), childbirth (n=1), IDU (n=1) and malignancy (n=1). An iGAS case requiring surgery could have more than one risk factor. No risk factors were identified for seven patients.

Intensive care unit (ICU) admission was required for 36 patients (24%), with an age range = 11 months – 88 years. Of those, 15 were notified as STSS, four as necrotising fasciitis and three as having both STSS and necrotising fasciitis. Risk factor data on 31 of the ICU cases (86%) was described, with age ≥65 years (n=16), skin and wound lesions (n=12), malignancy (n=5), steroid use (n=4), varicella infection (n=4), diabetes mellitus (n=3), alcoholism (n=2) and IDU (n=2). An iGAS case requiring ICU admission could have more than one risk factor. No risk factors were identified for six patients. Length of ICU stay was provided for 22 cases (61%); median = 3 days (range = 1 – 15).

Outcome

Outcome at seven days following GAS detection was reported for 74 cases (50%):

- Still alive = 70
- Died = 4, where GAS was listed as the main or contributory cause of death. The seven-day case fatality rate (CFR) for iGAS overall was 5%. Of 25 STSS cases, outcome at seven days was reported for 15 cases, with two deaths due to GAS (CFR = 13%)

Antimicrobial susceptibility testing

Twenty-eight microbiology laboratories reported antimicrobial susceptibility test (AST) data on 119 GAS isolates (blood; 110 and other specimens; 9) via the European Antimicrobial Resistance Surveillance Network (EARS-Net), with variation in AST panels. All isolates tested were susceptible to penicillin (n=119) and vancomycin (n=91). Resistance to erythromycin was reported in eight (7%) of 116 isolates, to clindamycin in seven (8%) of 89 isolates and to tetracycline in eight (13%) of 61 isolates tested.

Other epidemiological information

Seven cases of iGAS were reported as hospital-acquired (5%). There were no iGAS outbreaks reported in 2016 versus one outbreak in 2015.

Conclusion

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

Invasive GAS is a potentially life-threatening disease. In 2016, the CFR for iGAS infection was 5%.

A national service typing GAS *emm* genes has been provided since 2012 by the Irish Meningitis and Sepsis Reference Laboratory (IMSRL), based at Temple Street Children's University Hospital. In both 2016 and 2015 *emm*1 predominated, comprising 40% and 29% of all isolates typed, respectively. However, in 2014, *emm*3 predominated (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

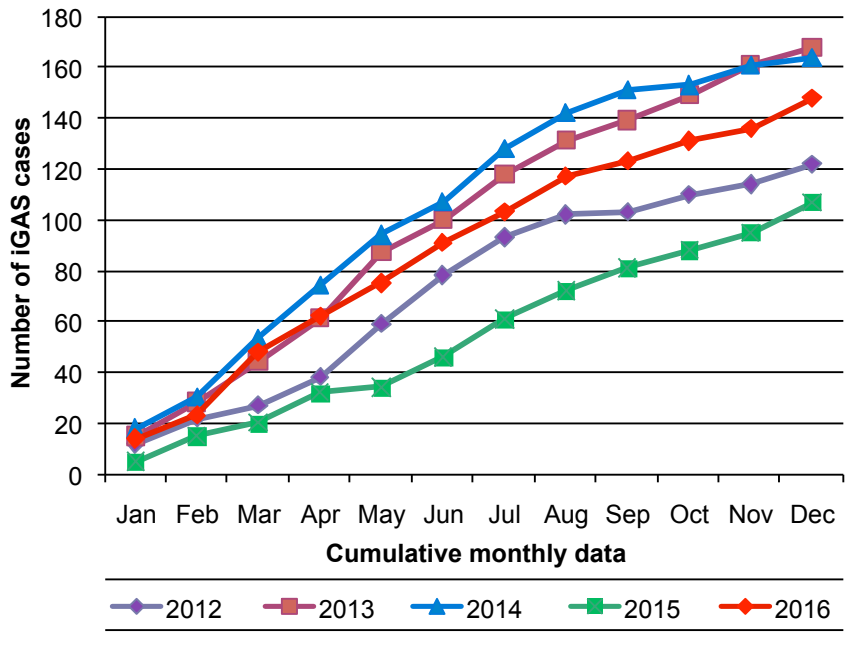

Figure 3. Cumulative monthly numbers of iGAS cases, 2012-2016

Table 2. Characteristics of iGAS cases (2012–2016) Data as of 16/08/2017

	2012	2013	2014	2015	2016
Notifications					
Total iGAS cases notified	122	168	164	107	148
iGAS incidence rate per 100,000 population	2.66	3.66	3.44	2.25	3.11
*Cases for which enhanced data provided** (%)*	*106 (87%)*	*156 (93%)*	150 (91%)	*95 (89%)*	120 (81%)
Patient Demographics					
Male (%)	59 (48%)	95 (57%)	94 (57%)	*60 (56%)*	77 (52%)
M:F ratio	0.94:1	1.30:1	1.34:1	*1.28:1*	1.08:1
Mean age	44	41	43	*42*	44
Median age	42	40	44	*42*	43
Age range	0-92	0-93	0-99	*0-99*	0-92
Paediatric cases (aged <18 years) (%)	28 (23%)	45 (27%)	47 (29%)	*26 (24%)*	40 (27%)
Older cases (aged 65+ years) (%)	42 (34%)	50 (30%)	56 (34%)	*34 (31%)*	52 (35%)
Clinical Presentation†					
Data on Clinical Presentation (%)	102 (84%)	141 (84%)	133 (81%)	*88 (82%)*	111 (75%)
Streptococcal Toxic Shock-like Syndrome (STSS) without NF (%)	22 (22%)	28 (20%)	18 (14%)	*11 (13%)*	22 (20%)
Necrotising fasciitis (NF) without STSS (%)	2 (2%)	6 (4%)	4 (3%)	*5 (6%)*	2 (2%)
STSS and NF (%)	4 (4%)	4 (3%)	3 (2%)	*0 (0%)*	3 (3%)
Bacteraemia with focal presentations (%)	37 (36%)	43 (30%)	43 (32%)	*33 (38%)*	43 (39%)
Bacteraemia with no focal presentations (%)	26 (25%)	37 (26%)	37 (28%)	*21 (24%)*	25 (23%)
Other focal presentations with no bacteraemia (%)	11 (11%)	23 (16%)	28 (21%)	*18 (20%)*	13 (12%)
Bacteraemia (%)	78 (76%)	106 (75%)	100 (75%)	*64 (73%)*	90 (81%)
Other focal presentations:					
Cellulitis (%)	40 (39%)	43 (30%)	57 (43%)	*34 (39%)*	50 (45%)
STSS (%)	26 (25%)	32 (23%)	21 (16%)	*11 (13%)*	25 (23%)
Pneumonia (%)	16 (16%)	24 (17%)	14 (11%)	*12 (14%)*	9 (8%)
Necrotising fasciitis (%)	6 (6%)	9 (6%)	7 (5%)	*5 (6%)*	8 (7%)
Septic arthritis (%)	7 (7%)	10 (7%)	10 (8%)	*13 (15%)*	7 (6%)
Peritonitis (%)	1 (1%)	4 (3%)	1 (1%)	*3 (3%)*	5 (5%)
Erysipelas (%)	3 (3%)	3 (2%)	2 (2%)	*1 (1%)*	2 (2%)
Myositis (%)	4 (4%)	3 (2%)	5 (4%)	*2 (2%)*	2 (2%)
Puerperal sepsis (%)	3 (3%)	4 (3%)	3 (2%)	*6 (7%)*	2 (2%)
Meningitis (%)	1 (1%)	3 (2%)	0 (0%)	*4 (5%)*	0 (0%)
Risk Factors†					
Data on risk factors (%)	95 (78%)	138 (82%)	126 (77%)	*77 (72%)*	93 (62%)
Skin lesions/wounds (%)	34 (36%)	56 (41%)	50 (40%)	*32 (42%)*	38 (41%)
Malignancy (%)	10 (11%)	23 (17%)	10 (8%)	*6 (8%)*	16 (17%)
Diabetes (%)	5 (5%)	16 (12%)	11 (9%)	*7 (9%)*	10 (11%)
Varicella (%)	8 (8%)	5 (4%)	6 (5%)	*3 (4%)*	8 (9%)
Steroid use (%)	8 (8%)	11 (8%)	6 (5%)	*6 (8%)*	8 (9%)
Injecting drug user (%)	6 (6%)	5 (4%)	5 (4%)	*3 (4%)*	4 (4%)
Childbirth (%)	6 (6%)	6 (4%)	4 (3%)	*5 (6%)*	3 (3%)
Alcoholism (%)	5 (5%)	6 (4%)	5 (4%)	*3 (4%)*	2 (2%)
Non-steroid anti-inflammatory drug use (%)	2 (2%)	4 (3%)	2 (2%)	*1 (1%)*	2 (2%)
No identified risk factor (%)	25 (26%)	47 (34%)	48 (38%)	*24 (31%)*	27 (29%)
Outcome at 7 days					
Data on outcome at 7 days (%)	65 (53%)	108 (64%)	102 (62%)	*73 (68%)*	74 (50%)
RIP/GAS main cause or contributory (%)	8 (12%)	16 (15%)	10 (10%)	*6 (8%)*	4 (5%)
STSS cases: Data on outcome at 7 days (%)	17 (65%)	26 (81%)	17 (81%)	*7 (64%)*	7 (64%)
STSS cases: RIP/GAS main cause or contributory (%)	6 (35%)	10 (38%)	6 (35%)	*1 (14%)*	1 (14%)
Severity					
Data on admission to ITU (%)	99 (81%)	153 (91%)	144 (88%)	*92 (86%)*	112 (76%)
Admitted to ITU (%)	40 (40%)	44 (29%)	36 (25%)	*25 (27%)*	36 (32%)
Data on surgical intervention (%)	85 (70%)	136 (81%)	127 (77%)	*86 (80%)*	99 (67%)
Surgical intervention required (%)	25 (29%)	39 (29%)	41 (32%)	*26 (30%)*	28 (28%)
Typing					
iGAS isolates that were typed (%)	109 (89%)	140 (83%)	130 (79%)	*92 (86%)*	127 (86%)
Emm-1 (%)	53 (49%)	41 (29%)	21 (16%)	*27 (29%)*	51 (40%)
Emm-3 (%)	4 (4%)	33 (24%)	47 (36%)	*4 (4%)*	6 (5%)
Emm-12 (%)	11 (10%)	4 (3%)	6 (5%)	*14 (15%)*	14 (11%)
Emm-28 (%)	8 (7%)	8 (6%)	12 (9%)	*12 (13%)*	10 (8%)
Emm-89 (%)	4 (4%)	13 (9%)	8 (6%)	*8 (9%)*	6 (5%)
Other *emm*-types (%)	29 (27%)	41 (29%)	36 (28%)	*27 (29%)*	40 (31%)

** 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

circulation 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. There has been a reduction in the proportion of iGAS cases with accompanying enhanced surveillance data from 93% (2013) to 81% (2016). Referral of GAS isolates to IMSRL for epidemiological typing is also important, as certain *emm* types are associated with greater morbidity and mortality.

Acknowledgement
HPSC would like to thank colleagues in microbiology laboratories and Departments of Public Health for submitting data on iGAS and colleagues in IMSRL for sharing *emm* typing information.

Notes to colleagues in microbiology laboratories

1. Please forward any GAS isolates from normally sterile sites to IMSRL for typing, along with a completed IMSRL request form available from: https://www.cuh.ie/wp-content/uploads/2014/03/IMSRL-Request-Form-29-11-16.pdf
2. Please submit AST data on all iGAS cases along with EARS-Net quarterly returns
3. Please return a completed enhanced iGAS surveillance form on every patient with iGAS. The form can be downloaded from the HPSC website at: http://www.hpsc.ie/a-z/other/groupastreptococcaldiseasegas/surveillanceforms/