CONGENITAL SYPHILIS QUARTERLY SURVEILLANCE REPORT
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INTRODUCTION

In order to monitor progress towards the elimination of congenital syphilis (CS), South Africa has included CS on its revitalised national Notifiable Medical Conditions (NMC) surveillance platform since July 2017. CS is a category 2 NMC- which means all health care workers are required to notify cases through paper-based or electronic case notification forms (CNF) within 7 days of diagnosis. In addition, data on clinical notifications collected through CNFs on the NMC platform, data on RPR positive results among infants and children < 2 years are collected in order to monitor maternal syphilis exposure and or testing practices. Since 1 January 2020, CS surveillance data are supplemented by collection of additional clinical information on notified cases through a CS specific case investigation form (CIF). This report presents data on clinical notifications and RPR positive results among infants < 24 months for the period 1 July 2017 – 31 December 2020. The report also presents data on gaps in congenital syphilis prevention and management using data from the newly introduced CIF.

METHODS

Data collection

The CS surveillance team at the Centre for HIV and STIs extracts data on notified cases and RPR positive results from infants/ children < 2years from the NMC system for case classification and analysis. Health care providers use a standard NMC case notification forms (CNF) to notify cases. Beginning January 2020, the Centre has been requesting notifying facilities to submit a case investigation forms (CIF) along with the CNF. This CIF collects additional information on maternal and infant clinical history. This additional information was meant to allow the Centre to: i) verify whether notified cases meet the case definition for early congenital syphilis and ii) identify gaps in the prevention and management of congenital syphilis. The report presents data collected during the period 1 July 2017 – 31 December 2020.

Data management and analysis

Data collected using the CNF was captured into the CS syphilis line list while CIFs were captured into an Excel spreadsheet. The data from the two sources were cleaned and matched for analysis. Matching was done using case notification number generated at submission of a clinical notification. Descriptive statistics were used to describe trends in clinical notifications by calendar quarter, district and province as well as maternal and infant characteristics of the notified cases. Since not all case notifications could be matched to a CIF, a sub-group analysis of cases who had both a CNF and CIF submitted was conducted and results compared to those from all CIFs received.

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RESULTS

In the period 1 July 2017 – 31 December 2020, there were a total of 794 clinical notifications of CS cases and 11 170 RPR positive results from infants/ children < 2 years. Over this period there was a steady increase in the both the number of clinical notifications and the number of RPR positive results from infants/ children (see Figure 1 and Table 1). Clinical notifications of CS cases were received from 114 facilities in 40 districts during this period.

In the most recent quarter (October – December 2020), the Centre received 77 clinical notifications from 23 facilities in 17 districts and 968 RPR positive results from infants < 2 years. This was compared to 88 clinical notifications from 24 facilities in 15 districts and 986 RPR positive results among infants < 2 years in the previous quarter.

Figure 1: Trends in CS clinical notifications and RPR positive specimens by quarter 1 July 2017 – 31 December 2020

* Dark green line- Number of clinical notifications received through the NMC platform by calendar quarter. NICD started coordinating the NMC programme and receiving clinical notifications mid-2017.

* Light green bars – Number of RPR positive results from infants/ children who are confirmed to be < 24 months at specimen collection by calendar quarter collected from the laboratory (via NICD Surveillance Data Warehouse).

* The dotted blue line is the trend line for notified cases assuming a linear relation between clinical notifications and calendar quarters

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Table 1: CS clinical notifications by calendar quarter, district and province July 2017-December 2020

District	Province	Q3,Q4 17	Q1 18	Q2 18	Q3 18	Q4 18	Q1 19	Q2 19	Q3 19	Q4 19	Q1 20	Q2 20	Q3 20	Q4 20	Total
Alfred Nzo	EC							2							2
Buffalo City Metro	EC			1		1		2							4
Joe Gqabi	EC											1			1
Nelson Mandela Bay Metro	EC							1	1				1		3
O R Tambo	EC						1	2	1						4
Sarah Baartman	EC	2	2	1			1					1			7
Fezile Dabi	FS								3		1				4
Mangaung Metro	FS	1	2	4	1	1	1	1						2	13
Thabo Mofutsanyana	FS											2			2
Xhariep	FS				1									1	2
City of Johannesburg Metro	GP	4	4	2	2		9	6	4	4	9	6	4	7	61
City of Tshwane Metro	GP			1	2		7	7	6	6	3	2	4		38
Ekurhuleni Metro	GP		2	1	6	13	5	13	4	7	5	28	10	8	102
Sedibeng	GP											3			3
West Rand	GP						2								2
Amajuba	KZN					6	1	6	5	10	6	6	3	8	51
eThekwini Metro	KZN	1		8	7	12	8	8	8	7	9	7	9	6	90
Harry Gwala	KZN				1										1
iLembe	KZN					1	1	5	2	7	16	31	16	21	100
King Cetshwayo	KZN	2	8	1	1		1	1	1	1	7	1	1	1	26
Ugu	KZN	1				1					1	2	2	2	9
uMgungundlovu	KZN	2		1	2	9	13	12	16	9	6	10	4	1	85
uMkhanyakude	KZN				1			1		1					3
Umzinyathi	KZN	5						1							6
uThukela	KZN	1						2	4	3	2	4			16
Zululand	KZN			3			3		5	5	1	1			18
Capricorn	LP							1				1			2
Waterberg	LP						2	1			1	1			5
Gert Sibande	MP											2			2
Nkangala	MP	1												1	2

District	Province	Q3,Q4 17	Q1 18	Q2 18	Q3 18	Q4 18	Q1 19	Q2 19	Q3 19	Q4 19	Q1 20	Q2 20	Q3 20	Q4 20	Total
Bojanala Platinum	NW											1	6	3	10
Dr Kenneth Kaunda	NW	1	2				2				2				7
Frances Baard	NC					4				1				1	6
Namakwa	NC					1									1
ZF Mgcawu	NC								1	2	1	7	1	2	14
Cape Winelands	WC				1		1		1		2	10	18	2	35
City of Cape Town Metro	WC	4		2		2	1	3		2	1	5	7	9	36
Eden	WC		4	1	1		1		1		1		2		11
Overberg	WC						2								2
West Coast	WC									4	2			2	8
Total notifications	**All**	**25**	**24**	**26**	**26**	**51**	**62**	**75**	**63**	**69**	**76**	**132**	**88**	**77**	**794**
Number of districts notifying	**All**	**12**	**7**	**12**	**12**	**11**	**19**	**19**	**16**	**15**	**19**	**22**	**15**	**17**	**40**
Number of facilities	**All**	**16**	**7**	**17**	**17**	**18**	**29**	**31**	**27**	**21**	**27**	**38**	**24**	**23**	**114**

Gaps in CS prevention and management

During the period 1 January – 31 December 2020, there were 373 clinical case notifications received. In the same period, there were 324 CIFs completed of whom 303 had case notification number listed. Of these, it was possible to match 175 CNF to CIF data using the case notification number alone. Figure 2 shows the distribution of the CNFs and CIFs submitted.

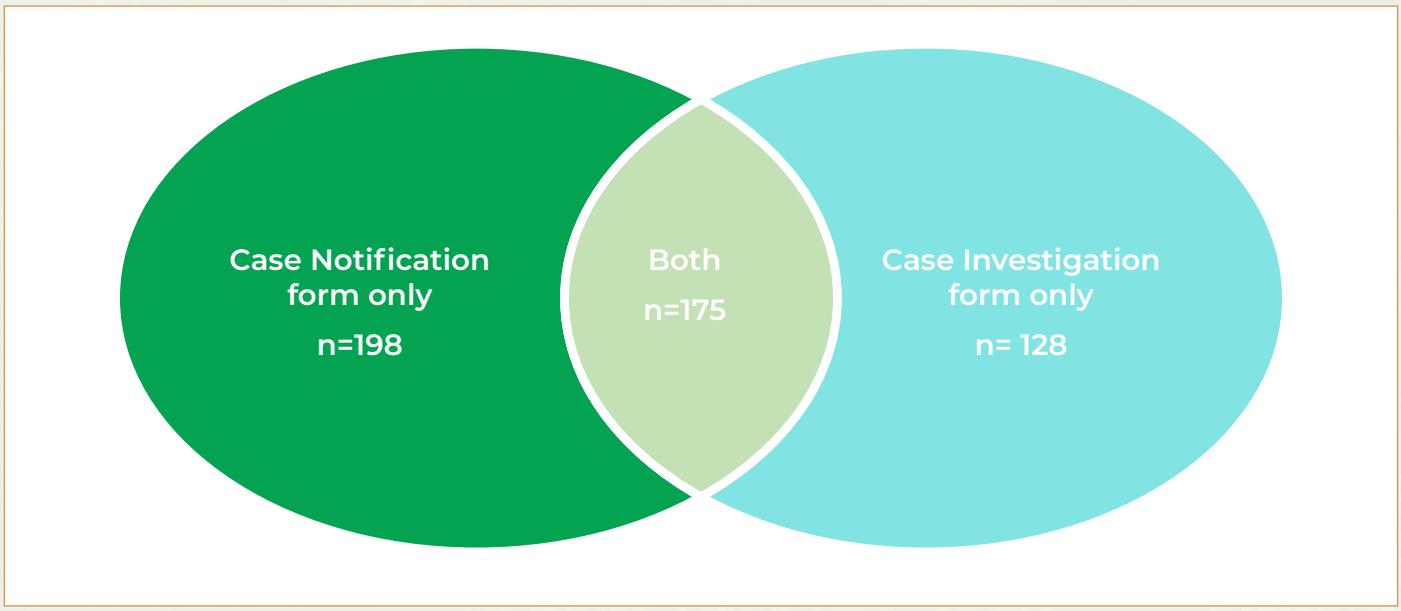

Figure 2: Distribution of CIFs and CNFs submitted to the NMC platform, 1 January – 31December 2020

Table 2 shows maternal characteristics of notified cases who had CIF data available. The majority of mothers were tested for syphilis during pregnancy with an RPR test (269/303, 88.8%). The majority of mothers were RPR positive (234/303, 77.2%) either during pregnancy or at infant diagnosis. The median RPR titre was 32 (8- 32) for the 175 for whom these data were available. Of those who were RPR positive during pregnancy or at infant diagnosis (n=234), 194 (82.9%) received treatment for syphilis with <5% not treated with Benzathine penicillin 2.4 MU. Overall 64.0% (194/303) of mothers whose infants were notified as CS cases and had a case investigation form submitted had evidence of receiving the full prevention of mother-to-child transmission of syphilis cascade – that is being tested for syphilis, testing positive for syphilis and being treated with Bethanzine penicillin- the full maternal treatment cascade.

Table 2: CS clinical notifications by calendar quarter, district and province July 2017-December 2020

Characteristics	N	n (%)
Evidence of syphilis test prior to delivery	303	269 (88.8)
Documented syphilis result	303	262 (86.5)
RPR positive	303	234 (77.2)
RPR titre values , (median, IQR)*	175	32 (8- 32)
Time from RPR test to delivery, (median, IQR)*	158	37.5 (2- 129)
Time from RPR test to delivery < 28days	158	68 (43.0)
One or more doses of Benzathine penicillin or equivalent received	303	200 (66.0)
Inadequate treatment – Ceftriaxone/ Amoxycillin with probenecid	200	6 (3.1)
Tested , received results and treated with at least one dose of Benzathine penicillin	303	194 (64.0
Documented HIV test	303	265 (87.5)
Maternal HIV test results positive	265	97 (36.6)
Gestational age at delivery in weeks (median, IQR)*	260	37 (33.5- 39)
Preterm delivery (delivery prior to 37 weeks of gestation)	260	108 (41.5)

*IQR = interquartile range

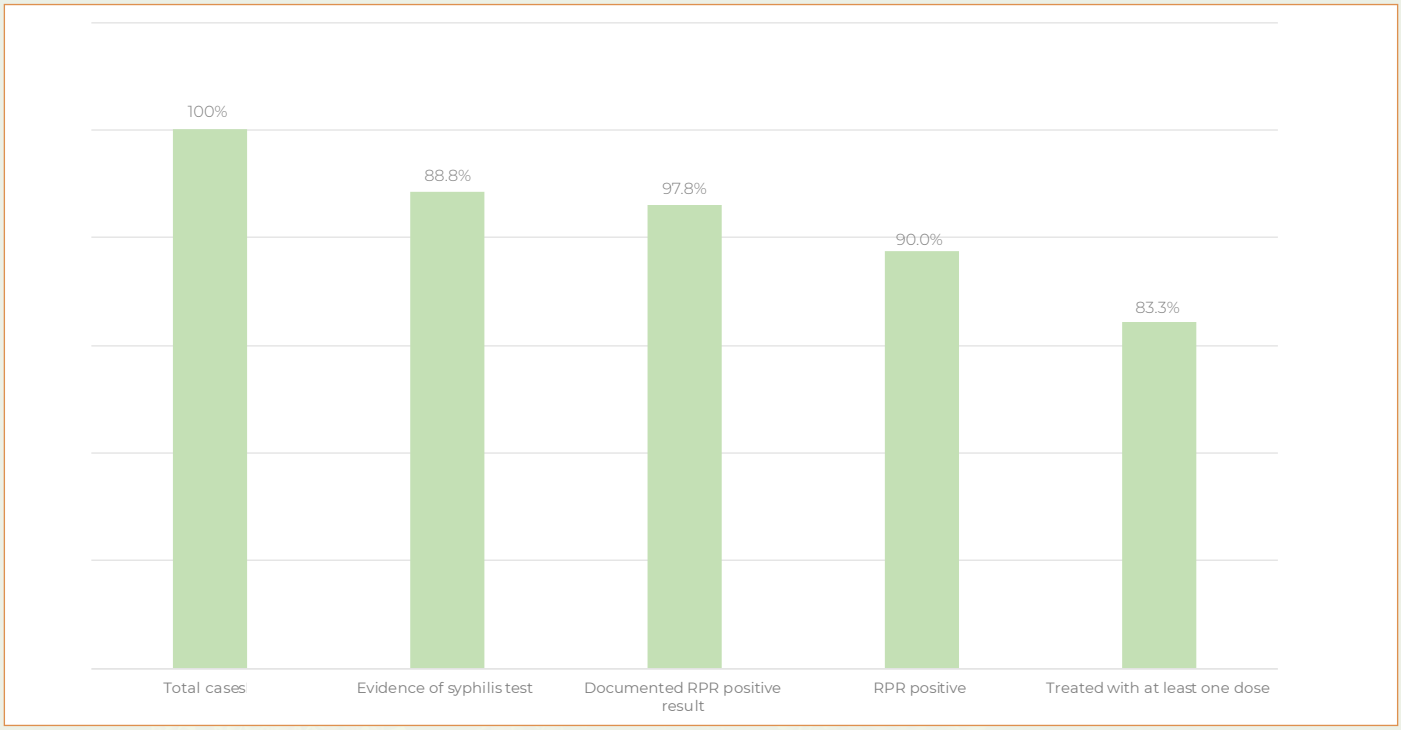

Figure 3: Prevention of mother to child transmission of syphilis care cascade for mothers of notified CS cases who had a CIF submitted to the NICD in 2020, N=303

*Percentages are presented as percentage of the previous column

Figure 3 shows the maternal syphilis care cascade for mothers of the notified cases. This shows that the majority of mothers whose infants had mother to child transmission of syphilis received testing for syphilis, that most of those who were tested had results documented with the majority being RPR positive. Just over 80% of those who were RPR positive were treated with at least one dose of Benzathine penicillin

Of the 209 mothers for whom HIV results were available, 36.6% where HIV positive, a positivity rate that was higher than the national ANC estimates of ~30%. The median gestational age at delivery was 37 weeks (33.5- 39 weeks) overall. About 42% of the mothers had a preterm delivery at a median gestational age of 32 weeks (31- 35 weeks).

Mothers of CS cases who had both CNF and CIF forms matched were less likely to have been tested, received results and treated with at least one dose (46.3% vs 59.4%, p=0.025) compared to those who did not have a CNF matched to a CIF. The rest of the maternal characteristics did not differ between cases who had a matching CNF and those who did not.

Table 3: Infant characteristics of notified CS cases who had CIF submitted to the NICD

Characteristics	N	n (%)
Age at notification in days, (median, IQR)	296	4 (2- 12)
RPR positive	303	263 (86.6)
RPR titer values, (median, IQR)*	236	16 (4- 32)
Clinical signs present	291	111 (38.1)
Radiological changes in long bones	281	21 (7.5)
Treatment with benzathine penicillin received	298	289 (97.0)
Stillbirth or neonatal death	167	5 (3.0)

Among the infants whose clinical information was available, the median age at notification was 4 days (2- 12 days). At notification, the majority were RPR positive with median titre levels of 16 (4- 32). Less than half of the infants (38.1%) notified had clinical signs and symptoms. Among the cases reported, radiological findings were less frequent as were stillbirths or neonatal deaths. Five infants either died or were stillborn.

DISCUSSION

This report presented data on clinical notifications submitted to the NICD as well as the clinical data collected through the newly introduced CIF. During the most recent quarter, there was a slight decrease in the number of congenital syphilis cases notified compared to the previous quarter. This was associated with a corresponding reduction in the number of districts and facilities reporting cases compared to the previous quarter. There was also a slight decrease in the number of RPR positive results in the current surveillance period compared to the previous quarter. Under-reporting of cases from facilities continued to be a challenge as evidenced by the limited number of facilities and districts reporting cases during the quarter and districts which have not notified cases since NICD took over the coordination of the NMC platform in 2017.

Gaps in the prevention, management and treatment of maternal syphilis resulted in mother to child transmission of syphilis. From this analysis:

- 11.2% of notified cases who had clinical information available had no evidence of a syphilis test. This could have been because of mothers being unbooked or that booking records were not available at the time of completion of the CIF. The relative contribution of each could not be determined, as there was no question about whether mother was booked or not on the CIF.
- 13% of those who were tested were RPR negative at initial test. These mothers could have acquired syphilis later in the pregnancy or had a false negative result. The CIF did not have data field to capture information on the retesting later in pregnancy and this will be amended in the next iteration of the form. The form did not collect information on whether the booking test was a rapid test or a laboratory-based test. There is no nationally validated algorithm and quality assurance programme for rapid syphilis tests in the country.
- For those RPR positive women for whom the data were available (N=158), the median time from test to delivery was close to a month, with 43% of the women delivering within 28 days of testing. Women who are tested and treated within four weeks of a syphilis diagnosis are considered inadequately treated. There is need to ensure that women book early, test and receive results and treatment early into their pregnancies.
- Of the mothers who were RPR positive, 17.7% had no evidence of treatment with Benzathine penicillin. This could be again because documentation was not available or results come back late that women are not treated. There is need to ensure that all women who test positive are treated as soon as possible. The planned introduction of the rapid test will improve the proportions of women tested who are treated
- Very few women whose infant outcome was CS received alternative regimens or medications (<5%). There is need for continued training of providers on what alternative regimens to use in case penicillin allergies.
- Approximately 64% of women whose infants were notified as CS cases received a test, received results and were treated with the correct regimens but still had infants with CS. It could be that the infants were notified in error or that the timing of the treatment was too late to prevent CS in the infant.

LIMITATIONS

Our analysis was subject to a number of limitations

- The notification system is dependent on health care workers identifying and notifying cases. There is under-notification of CS based on the limited number of facilities and districts submitting reports each quarter.

- Analysis of gaps in CS prevention is limited to infants who were diagnosed as CS and had CNF and CIF submitted. These children/infants may differ from those who are not notified. Those notified may have disease detected earlier and therefore have more favorable outcomes.

- The version of the CIF in use during 2020 did not have fields on booking status and 32 week re-testing. These variable/ data elements will be included in the next iteration of the form.

- Poor documentation or capturing of dates during reporting meant that timing of testing or treatment in relation to birth could not be determined for most women.

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