

Trisomy 21 screening with alpha software and FMF algorithm in South African private practice

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Objective

An audit was done to determine the test performance of antenatal screening for trisomy 21 using alpha and Fetal Medicine Foundation (FMF) software respectively in South African private practice.

Methods

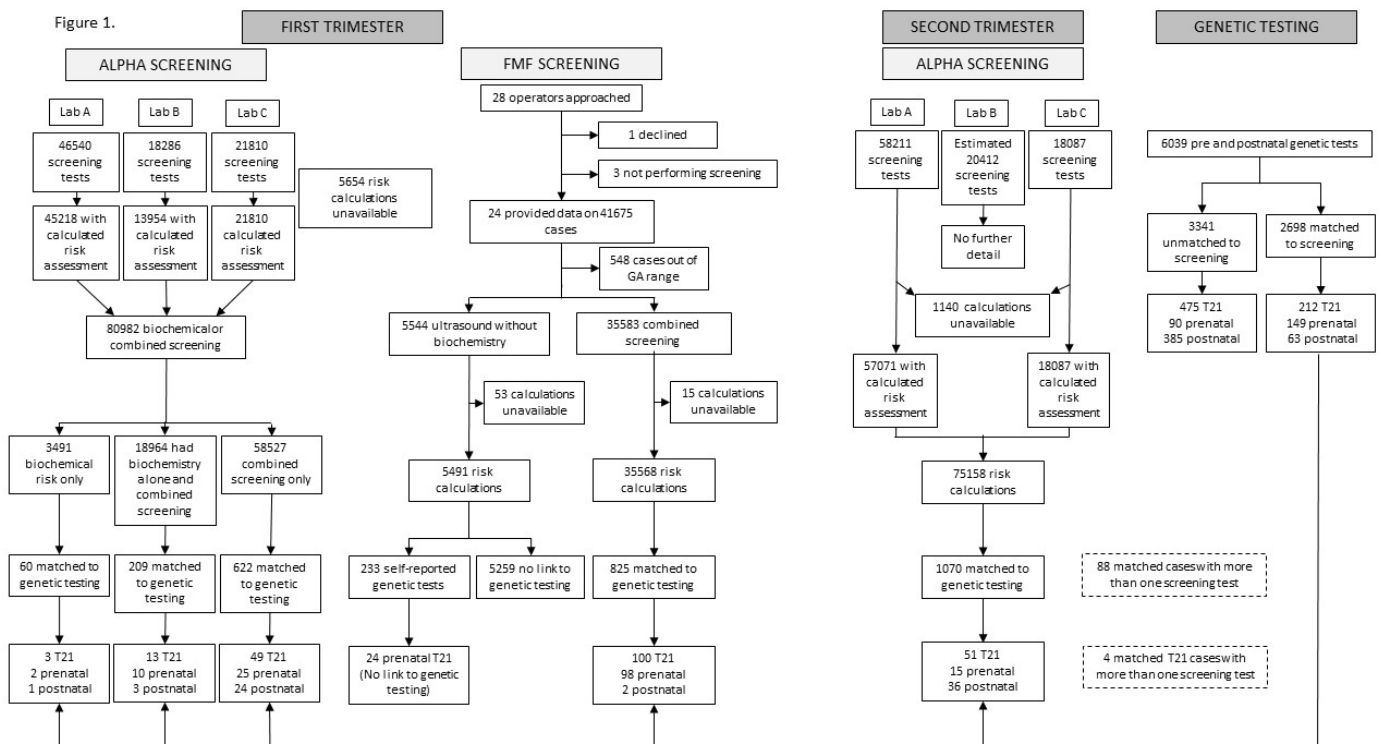
Screening data from 2010 to 2015 were retrospectively linked with pre- and postnatal genetic testing to assess screen positive and detection rates. First and second trimester biochemistry screening with alpha software, first trimester ultrasound screening with FMF software and combined first trimester biochemistry and ultrasound screening using alpha and FMF software respectively were compared.

Results

One third of pregnancies underwent screening. There were 687 trisomy 21 cases in 225021 pregnancies with 239 (35%) diagnosed prenatally. Screen positive rates were 11.8% for first trimester biochemistry, 7.6% for second trimester biochemistry, 7.3% for first trimester FMF software ultrasound, 3.5% for combined first trimester screening with alpha software and 3.7% for combined first trimester screening with FMF software. For a 5% screen positive rate, the detection rate was 63% for first trimester biochemistry, 69% for second trimester biochemistry, 80% for alpha combined first trimester software and 95% for FMF combined first trimester software.

Conclusion

Low detection rates are mainly due to a low prevalence of screening. Detection rates were highest if screened using FMF software.



Screen positive rate, positive predictive value for trisomy 21 and detection rate of trisomy 21 (with 95th percentile confidence intervals) with high-risk results at the time of screening (> 1:300 in the first trimester and > 1:270 in the second trimester), and detection rate for a fixed 5% false positive rate (cut-off for risk in square brackets). (95% confidence intervals in brackets).

	First trimester				Second trimester
	Alpha software		FMF software incl. NT		Alpha software
	Biochemistry only	Combined testing	Ultrasound only	Combined testing	Biochemistry only
Screen positive rate	2 639/22 455* 11.8 (11.3-12.2) %	2 737/77 491 3.5 (3.4-3.7) %	401/5 491 7.3 (6.6-8.0) %	1 308/35 568 3.7 (3.5-3.9) %	5 752/75 158 7.7 (7.5-7.8) %
<i>Maternal age < 35 yr</i>	1279/18408 6.9 (6.6-7.3) %	1 104/63 188 1.7 (1.6-1.8) %	282/4 182 6.7 (6.0 – 7.5) %	590/24 704 2.4 (2.2-2.6) %	2 297/61 437 3.7 (3.6-3.9) %
<i>Maternal age ≥ 35 yr</i>	1 419/4 012 35.4 (33.9-36.8) %	1 629/14 220 11.5 (10.9-12.0) %	114/1 222 9.4 (7.9-11.2) %	718/10 861 7.2 (6.7-7.7) %	3 797/13 648 27.8 (27.1-28.6) %
Positive predictive value	15/203 7.4 (4.5-11.9) %	49/510 9.6 (7.3-12.5) %		94/445* 21.1 (17.6 – 25.2) %	38/854 4.5 (3.2 – 6.1) %
<i>Maternal age < 35 yr</i>	3/68 4.4 (10.1-12.7) %	14/210 6.7 (3.9-11.0)		32/246* 13.0 (9.3-17.8) %	8/330 2.4 (1.2-4.8) %
<i>Maternal age ≥ 35 yr</i>	12/135 8.9 (5.0-15.0)	35/300 11.7 (8.5-15.8)		62/199* 31.2 (25.1-37.9) %	30/524 5.7 (4.0-8.1) %
Detection rate for high risk result	15/16 93.8 (69.7 to > 99.9) %	49 / 62 79.0 (67.2 – 87.5) %		94/100 94.0 (87.3 -97.5) %	38/51 74.5 (61.0 – 84.5) %
<i>Maternal age < 35 yr</i>	3 / 4 75 (28.9-96.6) %	14/26 53.9 (35.5-71.3) %		32/37 86.5 (71.6-94.6) %	8/19 42.1 (23.1-63.8) %
<i>Maternal age ≥ 35 yr</i>	12/12 100.0 (71.8-100.0) %	35/36 97.2 (84.6->99.9) %		62/63 98.4 (90.7->99.9) %	30/32 93.8 (78.8-99.3) %
Detection rate at 5% screen positive rate	10/16 62.5 (38.5-81.6) % [1:110]	50/62 80.1 (70.3-89.3) % [1: 440]		95/100# 95 (88.5-98.1) % [1:498]	35/51 68.6 (54.9-79.7)% [1:173]
<i>Maternal age < 35 yr</i>	1 / 4 25 (34.1-71.1) %	15/26 57.7 (38.9-74.5) %		33/37# 89.2 (74.7-96.3)	6/19 31.6 (15.2-54.2) %
<i>Maternal age ≥ 35 yr</i>	9/12 75 (46.2-91.7) %	35/36 97.2 (84.6->99.9) %		62/63 98.4 (90.7->99.9) %	29/32 90.6 (75.0-97.5)

NT: Nuchal translucency; yr: years*: Significantly different from all others with p ≤ 0.0001; #: Significantly different from all others with p < 0.05