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## Introduction

Infertility is the inability to conceive after a year of unprotected intercourse involving heterosexual partners. Approximately 40-50% of infertility is related to male owing to chromosome abnormalities and Y chromosome microdeletion within the Yq11.2 region. Our objective is to evaluate the frequency of chromosome abnormalities and Y-chromosome microdeletion (AZF region) in infertile men in Malaysia.

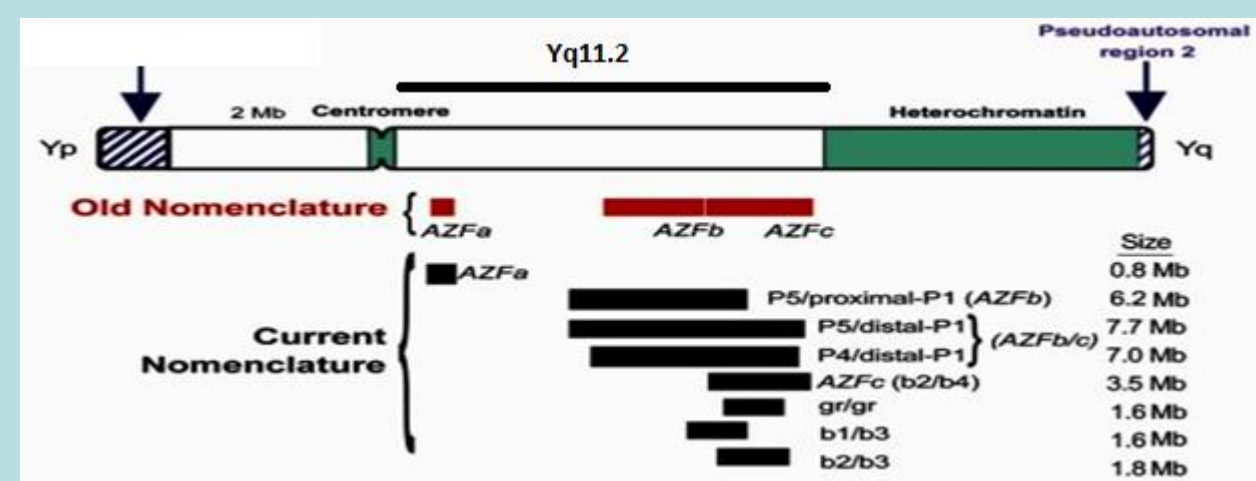
## Materials and methods

This was a retrospective study, based on the data of the Genetic Laboratory, Hospital Kuala Lumpur and Genetic Laboratory, Department of Pathology, Women and Children Hospital Kuala Lumpur (for the period 2015-2018). A total of 138 Malaysian infertile men (116 azoospermic, 5 oligospermic and 9 severe oligospermic) were screened for the presence of chromosomal abnormalities and Y chromosome microdeletion using conventional cytogenetic analysis and Multiplex Ligation-dependent Probe Amplification (MLPA) assay using MLPA probmix (P360). These test were carried out upon request from the treating clinician from various hospital.

## Results

Cytogenetic analysis of 107 men showed presence of chromosomal abnormalities in 15.9% (17/107) of cases, and all were seen in azoospermic men. Out of the 17 patients, 15 cases have sex chromosome abnormalities (88.2%), and the remaining 2 patients (11.8%) harboured autosomal chromosome abnormalities. The sex chromosome abnormalities include Klinefelter syndrome in 5 patients (29.4%).

Test	No. of patient
Cytogenetic Analysis only	47
MLPA analysis only	31
Cytogenetic Analysis and MLPA Analysis	60
<b>total</b>	<b>138</b>



Indication	Chromosomal Abnormality	no of patient
Azoospermia	47,XXY	2
Azoospermia	46,XX.ish Xp11.1q11.1 (DXZ1x2)	3
Azoospermia	46,X,inv(Y)(p11.2Q11.2)	1
Azoospermia	46,XX.ish der(X)t(X;Y)(p22.3;p11.3)(SRY+)DSD	1
Azoospermia	46,X,idic(Y)(q11.2).ish X(DXZ1x1), idic(Y)(q11.2)(SRY++)	1
Azoospermia	46,X,+mar[55]/45,X[45].ish X(DXZ1x1),idic(Y)(p11.3)(SRY++)/X(DXZx1,SRYx0)	1
<b>Total</b>		<b>9</b>

Indication	Yq microdeletions detected	No of patient
Azoospermia	AZFbc deletion (P5/distal P1)	1
Severe Oligospermia	AZFc deletion (b1/b3 deletion)	1
Azoospermia	AZFc deletion	2
Azoospermia	AZFc partial duplication with b1/b3 deletion	1
Azoospermia	Partial AZFc deletion : gr/gr deletion	1
Azoospermia	AZFc partial duplication	1
Azoospermia	deletion of AZF region (AZFa, AZFb and AZFc)	1
<b>Total</b>		<b>8</b>

Y-microdeletion were detected in 19.8% patients (18/91) (AZFc: 77.8% [14/18], AZFbc: 16.7% [3/18] and AZFabc: 5.5 % [1/18]) and the frequencies in patient subgroups with azoospermic, oligospermic and severe oligospermic were 83.3% (15/18), 0% (0/18) and 16.7% (3/18); respectively.

Indication	Chromosomal Abnormality	Yq microdeletions detected	No. of patients
Azoospermia	47,XY,+mar[8]/46,XY[22]	NORMAL	1
Azoospermia	46,XY,t(1;5)(p31;q35)	NORMAL	1
Azoospermia	46,XY,der(15)t(Y;15)(q11.23;p11.1).ish Y(wcpY+)	NORMAL	1
Azoospermia	47,XXY	NORMAL	2
Azoospermia	47,XXY	Partial AZFc deletion : gr/gr deletion	1
Azoospermia	46,X,+mar. ish X(p11.1q11.1)(DXZ1+), Y(p11.3)(SRY+)	AZFbc deletion (P5/distal P1)	1
Azoospermia	46,X,abnormalY.ish Xp11.1q11.1(DXZ1x1), Yp11.3(SRYx1)	AZFbc deletion (P5/distal P1)	1
Azoospermia	NORMAL	AZFc deletion	2
Azoospermia	NORMAL	Partial AZFc deletion : gr/gr deletion	1
Azoospermia	NORMAL	AZFc partial duplication with gr/gr deletion	1
Severe Oligospermia	NORMAL	AZFc deletion	1
Severe Oligospermia	NORMAL	Partial AZFc deletion : gr/gr deletion	2
<b>Total</b>			<b>15</b>

## Discussion / Conclusion

Chromosomal abnormalities and Y-chromosome microdeletion accounted for 23.2% infertility cases (32/138) among Malaysian men. These results highlighted the need for efficient molecular genetic testing in male infertility diagnosis. Genetic testing should be a routine examination in infertile males alongside genetic counselling prior assisted reproductive treatment.

## References

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