Introduction

Noninvasive Prenatal Testing (NIPT), also known as Cell-Free DNA (cfDNA) test, utilizes fetal DNA that is circulating in maternal blood to detect genetic anomalies within a fetus. Aneuploidy is known as a notable problem in obstetrics and gynecology for female patients. Aneuploidy includes trisomy 21, trisomy 18, and trisomy 13, and these genetic abnormalities have increased the need for prenatal testing [1]. Invasive prenatal testing (IPT) is commonly performed for certain genetic abnormalities, such as trisomy 21, trisomy 18, and trisomy 13 [2]. A common risk associated with this procedure is miscarriage. Noninvasive prenatal testing (NIPT) provides a safer alternative compared to invasive prenatal testing (IPT) for many women [3].

Methodology

Literature utilized in this review needed to be recent (published within the last 5 years), a primary study (a clinical trial or another experimental work), and discuss the overall effectiveness of cfDNA in screening SCAs. Ideal studies included statistical analysis on the effectiveness of cfDNA in screening SCAs and discussed the limitations of widely adopting the cfDNA technique in clinical practice. Studies that assessed the effectiveness of cfDNA for other purposes were excluded. The data collected for review included the specific screening information, methods being used, the PPV, NPV, FN, FP, the sample population, and any challenges, limitations, and biases reported in the study. All of which contribute to the feasibility of cell free fetal DNA as a primary screening method.

Article Selection

Identification

Records identified after abstract screening

Records excluded by abstract screening

Records included in systematic literature review

Studies included in systematic literature review

Note. Literature were obtained via PubMed using specific key words. Literature were included or excluded based on specific criteria (as listed below) using abstract during the first screening and abstract/full body review during second screening. 13 studies were included in the final review.

Strengths

- Utilizes recent studies and primary research
- Focuses on statistical evidence to determine the effectiveness of NIPT
- Variation in sample (gestational age, cap off of ≥10 weeks, risk groups (low, intermediate, high))
- Provides background on cfDNA and NIPT, and compares and contrasts to traditional invasive methods
- Discusses future application and limitations

Limitations

- Insufficient time to review every clinical study that was within the search, narrowed to 13 articles
- First time through meta-review process
- Focused search through PubMed
- Inconsistent statistics of SCA

13 Studies’ PPV

Table 1

Analysis of the PPV of various types of sex chromosome abnormalities across 13 studies

<table>
<thead>
<tr>
<th>Sex Chromosome Aneuploidies</th>
<th>PPV (%)</th>
<th>46,XY</th>
<th>46,XX</th>
<th>46,XY (Turner Syndrome)</th>
<th>47,XXY</th>
<th>47,XXX</th>
</tr>
</thead>
<tbody>
<tr>
<td>46,XY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.97</td>
<td>0.84</td>
</tr>
<tr>
<td>46,XX</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.97</td>
<td>0.84</td>
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<td>0.84</td>
</tr>
</tbody>
</table>

Note. Statistics show inconsistencies in PPV for different sex chromosome aneuploidies across 13 studies. Lowest PPV is seen in monosity X and highest PPV is seen in XXY. Not much statistical data provided for 45,XY, Overall, combined-PPV for SCA is low. Thus low accuracy, potential PPV, in different conditions, and sensitivity have kept the limited effectiveness of NIPT for SCAs. Where one study may say the PPV range is moderately accurate, therefore the clinical use of NIPT is recommended, another study says that the PPV range accuracy is low and thus the clinical use of NIPT for SCA is not recommended. Although NIPT for SCAs has positive implications in clinical practice, more methodological improvement is needed to improve its detection accuracy.

Future Directions

- Establishing baseline of PPV for SCAs
- Evolving technology to increase detection accuracy of SCAs and utilization as a diagnostic tool
- To make cfDNA testing more cost-effective and convenient
- Looking into utilizing cfDNA as treatment of genetic diseases in the unborn

Conclusion

Despite high specificity and sensitivity for SCAs, studies have inconsistent but low PPVs with a combined SCAs’ PPV of 46.08%, thus demonstrating low effectiveness of NIPT for SCAs. SCAs, considering their high rates (48-50%) which is consistent with most of our sources (Guo, 2022). The data compiled from those sources has an average PPV of 46.08% across the 13 studies reviewed. The studies reviewed seemed to have different minimum criteria to designate the effectiveness of NIPT for SCAs. Where one study may say the PPV range is moderately accurate, therefore the clinical use of NIPT is recommended, another study says that the PPV range accuracy is low and thus the clinical use of NIPT for SCA is not recommended. Although NIPT for SCAs has positive implications in clinical practice, more methodological improvement is needed to improve its detection accuracy. Genetic counseling is needed following a positive NIPT to ensure subsequent confirmatory tests are carried out, to ensure that prospective parents fully understand the diagnosis and make an informed decision.

References