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An Analytical Study on Screening Methods of Foetal Abnormalities Associated with Alpha-Fetoprotein Level

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Abstract
Adopting scoping review approach, this article aims to conduct an analytical study on screening methods of foetal abnormalities associated with Alpha-Fetoprotein (AFP) level, which is defined as plasma protein produced by the foetus. The issue of foetal abnormalities associated with AFP levels is increasingly getting serious. The risk of adverse pregnancy outcomes (APOs) is significantly higher in the group of women with abnormal level of maternal serum-alpha fetoprotein (MS-AFP) than in women with normal MS-AFP. According to recent research findings, the spontaneous abortion, structural foetal abnormalities, and preterm birth has the highest occurrence rates of APOs. Applies the scoping review approach, this article aims analyze the screening methods on foetal abnormalities associated with AFP levels. The main purpose of the study is to provide a holistic view on screening method. This holistic approach comprises various analytical aspects, including data analysis and evaluation of the screening methods. The study is anticipated to provide an effective method of understanding how screening methods can contribute in clarifying problems of foetal abnormalities linked with AFP levels.
Keywords: alpha-fetoprotein, analytical approach, maternal screening, foetal abnormalities, down syndrome, scoping review.

Abstrak
Mengguna pakai pendekatan semakan skop, artikel ini bertujuan untuk menjalankan kajian analitik mengenai kaedah saringan keabnormalan janin yang dikaitkan dengan tahap Alpha-Fetoprotein (AFP), yang ditakrifkan sebagai protein plasma yang dihasilkan oleh janin. Isu keabnormalan janin yang dikaitkan dengan tahap AFP semakin serius. Risiko hasil kehamilan yang buruk (APO) adalah jauh lebih tinggi dalam kumpulan wanita dengan tahap abnormal serum-alpha fetoprotein (MS-AFP) ibu berbanding wanita dengan MS-AFP biasa. Menurut penemuan penyelidikan baru-baru ini, pengguguran spontan, keabnormalan struktur janin, dan kelahiran pramatang mempunyai kadar kejadian tertinggi APO. Dengan pendekatan semakan skop, artikel ini bertujuan menganalisis kaedah saringan keabnormalan janin yang berkaitan dengan tahap AFP. Tujuan utama kajian adalah untuk memberikan pandangan holistik mengenai kaedah saringan. Pendekatan holistik ini merangkumi analisis data dan penilaian kaedah saringan. Kajian ini dijangka menyediakan kaedah yang berkesan untuk memahami bagaimana kaedah saringan boleh menyumbang dalam menjelaskan masalah keabnormalan janin selari dengan kadar AFP.
Kata Kunci: alpha-fetoprotein, pendekatan analitikal, pemeriksaan ibu, keabnormalan janin, sindrom down, semakan skop.

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Introduction

It has been emphasized by Islamic teachings and scientific research that improvement in health care, food, and education can reduce the prevalence and phenotypic severity of several congenital abnormalities. Accordingly, prenatal genetic testing and reimplanting genetic diagnosis (PGD) are becoming necessary to reduce the frequency and severity of birth abnormalities (Paley Galst & Verp, 2015).

The issue of foetal abnormalities linked with Alpha-fetoprotein (AFP) levels is one of the major problems. AFP is plasma protein which develop mainly in the liver of the foetus, and also in the gastrointestinal (GI) tract and the yolk sac, a composition that exists throughout embryonic growth. A prominent mammalian oncofetal protein, AFP is a part of the superfamily of albuminoid genes, composed of serum albumin, vitamin D-binding protein, and chromosome alpha-albumin (afamin). In 1956, α-fetoprotein (AFP) was the first time been detected in human foetuses by Bergstrand and Czar (Van Houwelingen & Sandoval, 2016).

AFP is one of the biochemical markers which is targeted to detect membranes leakage in premature rupture of membranes (PROM). PROM is defined as the rupture of the foetal membranes before the beginning of labour at any gestational age (Ruanphoo & Phupong, 2015). The Amnioquick Duo+ (Biosynex, Strasbourg, France) is a novel noninvasive, rapid immunochromatographic test that was just released. This immunochromatographic test can identify the presence of two biological markers in the amniotic fluid: AFP and insulin-like growth factor-binding protein-1 (IGFBP-1). The IGFBP-1 (10 ng ml^{-1}) and AFP (5 ng ml^{-1}) thresholds have been specified for the test (Ruanphoo & Phupong, 2015).

AFP is found in monomeric as well as in dimeric and trimeric forms, and attaches copper, nickel, fatty acids, and bilirubin. It attaches the hormone estradiol in normal foetuses. Altered serum AFP rates have been identified in certain birth defects at the same time as abnormal development occurrences (Van Houwelingen & Sandoval, 2016). Low or high levels of AFP in the maternal may indicate a risk of Down Syndrome or neural tube defect (a severe disorder that causes aberrant development of a growing baby's brain and spine), twins or multiple births, and miscalculation of the due date. All these are the risky implications of AFP levels during pregnancy. (Adigun, Yarrarapu SNS, Khetarpal S., 2021).

There are various methods for screening of foetal anomalies during the first and second trimesters of pregnancy. For the first trimester, there are maternal blood screening and ultrasound, while for the second trimester, there are maternal serum screening, foetal echocardiogram and anomaly ultrasound. The second-trimester triple test [alphafetoprotein (α-FP), human chorionic gonadotrophin (hCG) or free b-hCG, and unconjugated oestriol (uE3)] are the most used screening test methods. A study by Li, et al. (2016) reported that there are two categories of screening tests performed during the first trimester combined screening, which are pregnancies screened with ‘low risk’ and ‘high risk’. Positive NIPT results were verified with karyotyping, whereas negative results were followed up on after delivery with an interview. During post-test counselling, the pregnant option based on non-invasive prenatal testing (NIPT) and confirmation results was addressed (Tan et al., 2016). Amniocentesis was conducted after NIPT positive results, followed by karyotyping and, if necessary, the therapy of multifetal pregnancy reduction (MFPR). Standard healthcare interventions were offered for NIPT negative resultsRecent

developments in antenatal screening programmes and intrauterine interventions have indicated that further details about the condition of the developing foetus may be accessed. (Dalrymple, 2012). Effectiveness of the screening methods in all this is crucial, but there also the problem of financial implication. Only relatively few people in developing countries can afford to utilise these screening methods. This study aims to analyse the screening methods of foetal abnormalities associated with abnormal AFP levels, based on scoping review approach. It investigates how these approaches can contribute to solving the problem.

2. Methodology

The scoping review approach is generally adopted in this article for data collection and analysis. The Joanna Briggs Institute Reviewers' Manual 2015 technique was applied to simplify the research and literature review procedure. The study protocol followed the method for determining primary studies based on proper analysis and causal factor characteristics. Basic information based on objectives, design, causative factors, and outcomes was gathered after critical evaluation of the articles. The primary components of the issue were used to define the search strategy planning, and natural language terminology were employed to describe the subject. The search was specifically focused on comparisons, results, analysis of findings, abstracts, and complete texts that covered the topic. The analytical method was used to examine screening cases of foetal abnormalities associated with aberrant AFP levels from the early 2000s to the present.

Theoretical understanding and research pertaining to foetal complications were incorporated in the selection criteria of the study for the concept and application. Analytical method was used to interpret the acquired theoretical and theoretical data. The study's selection criteria were centred on the diagnosis of foetal problems caused by an elevated AFP level in order to assess the efficacy of the application of analytical method on screening foetal abnormalities.

2.1. Research strategy

Finding the published research is the goal of the search strategy. To find relevant publications, an initial limited search of EBSCO Discovery Service (EDS), PubMed and Scopus were conducted. A comprehensive search technique was developed using the text words found in the titles, abstracts, and index keywords of pertinent papers. Each included database and/or information source will receive a customised version of the search strategy, which includes all indicated keywords and index terms. The first keywords used include "(foetal OR fetal OR foetus OR fetus OR babies OR baby OR infant OR infants OR prenatal) AND (defect OR defects OR abnormalities OR abnormality OR disabilities OR disability)". The second keywords are "alphafetoprotein" OR "alpha-fetoprotein" OR "(alpha fetoprotein)" OR "AFP" OR "afp". The exclude keyword is also presented to exclude unnecessary information which is "(neoplasia OR neoplasm OR cancer OR cancers)".

The general process of selecting the papers was done, it begins with removing the duplicates, screening the title and following by abstract. Then, the full-text articles will be retrieved and checked again for selection or removal by applying the inclusion and exclusion criterion. Finally, the remaining papers will be included in the study.

2.2. Data extraction and analysis

Specific information on the relevant papers, concept, context, research methods, and major findings that are pertinent to the review questions are included in the data that is extracted. A synthesis of the study's

characteristics and its findings are presented. The process of arranging the comparisons, planning the synthesis, carrying out the synthesis, analysing, and explaining the results is made by using the general framework for the synthesis. To aid in the analysis and comparison of all components across studies, the study characteristics were tabulated, allowing for the synthesis of all these characteristics.

2.3. Study selection

After screening, there are 13 articles which fulfil the criteria of the study, as in the following figure.

From the database and reference searches, 263 articles were identified. However, after removing the duplication of the study, the remaining articles turn 216. After screening the titles and abstracts, 157 records were excluded for reasons shown in Figure 2.3, and 30 articles were read in full to determine were read in full to determine eligibility. Of these, 17 articles were excluded because they did not meet the inclusion criteria. A total of 13 articles underwent full data extraction and are included in this review.

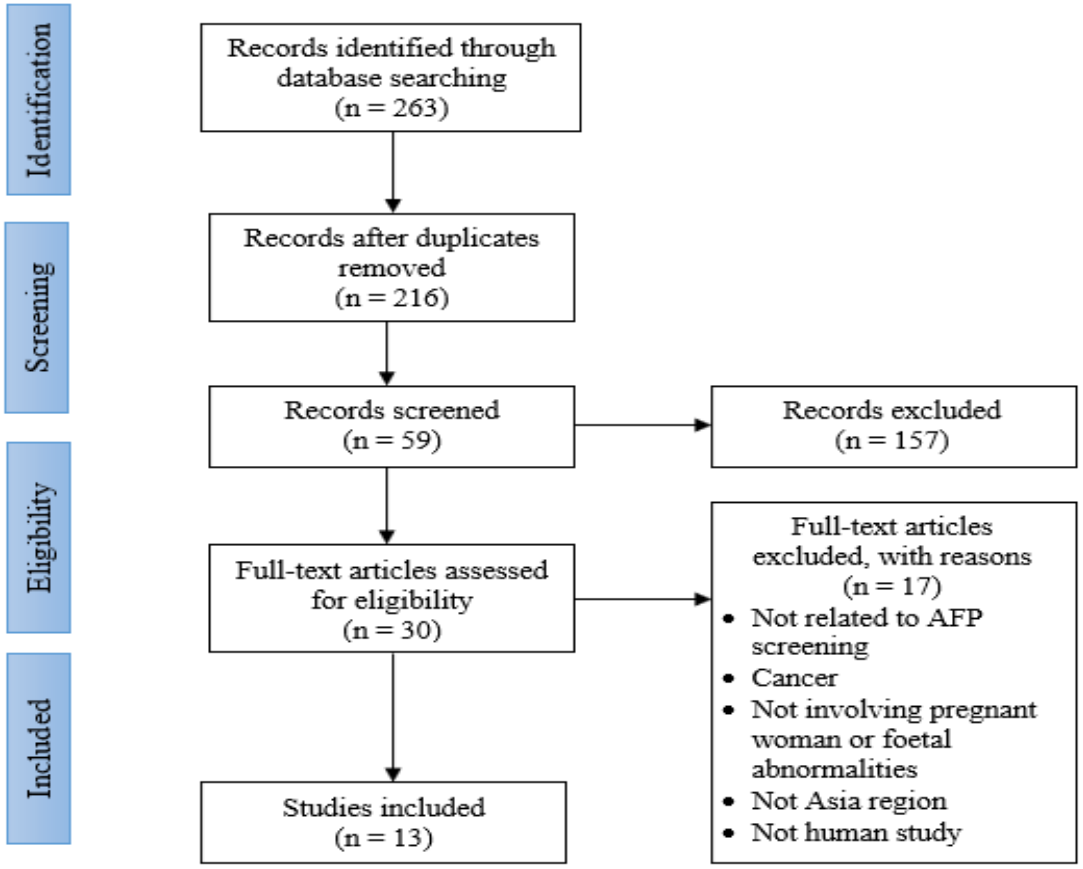

Figure 2.3 The studies included after the process of inclusion and exclusion criteria

Table 2.4: Full data extraction for included articles

Year of publication	**First author**	**Country of origin**	**Research methods**	**Aim/Subject matter**
2006	Wang	China	Cohort study	Analysing the relationship between maternal weight and maternal serum markers for Down syndrome screening
2006	Wang	China	Cohort study	Compare the performance of double screening and ethnic variance between Chinese and Caucasian populations
2007	Chen	China	Field survey and literature review	Cost-effectiveness of prenatal diagnosis intervention for Down's syndrome
2012	Miao	China	Cross-sectional study	Effectiveness of first trimester, second trimester, and integrated screening for Down's syndrome
2012	Wanapirak	Thailand	Cross-sectional study	Thai-specific reference ranges of triple markers for foetal Down syndrome
2016	Li	China	Cross-sectional study	Factors associated with utilization of MSS and the current status of service utilization in mainland China.
2016	Li	China	Prospective observational cohort study	Feasibility and performance of the first-trimeste

				r combined screening test for trisomy 21 in a resource-limited setting.
2016	Tan	China	Prospective study	Performance of noninvasive prenatal testing (NIPT) in twin pregnancies after the treatment of assisted reproductive technology (ART)
2016	Tu	China	Exhaustive literature search	Screening performance of PSMSUM in detecting Down Syndrome
2017	Du	China	Retrospective cohort study	Evaluation the value of absent foetal nasal bone in the prediction of foetal chromosomal abnormalities
2018	Li	China	Cohort study	Preterm birth rate factor
2021	Praikaew	Thailand	Cross-sectional study	Normative models for median levels of serum biomarkers of the second trimester quad test
2021	Pranpanus	Thailand	Prospective study	Efficacy of the quadruple test for potential use as a Thai national policy for Down syndrome (DS) screening.

3. The current screening methods

A prenatal diagnosis must be made if a pregnant woman has polyhydramnios or anhydramnios, abnormal foetal development or the foetus is suspected of malformation, early-pregnancy contact with a substance that could cause congenital defects, a family history of genetic diseases or a history of giving birth to an infant with a serious congenital defect or becoming a primipara

(having first child) at the age of 35 or beyond. (Zhu, 2013). The prevalence of DS in pregnant women 35 years and older, as well as the cost of prenatal diagnosis, affect the robustness of the maternal age screening method. The incremental cost-effectiveness ratio would fall if the rate of prenatal diagnosis was raised in both affirmatively screened women and women 35 years and older. In terms of effectiveness and cost-efficiency, most studies imply that serum screening is superior to age screening (Chen, 2007).

For the current worldwide diagnosis methods of foetal complications, there is implementation of a two-stage ultrasound screening method that integrates all patients with a routine of first and second-trimester ultrasound scan. However, recent developments in antenatal screening programmes and intrauterine interventions also indicated that further details about the condition of the developing foetus may be accessed. (Dalrymple, 2012). For the pregnant women who aged 35 years and older which are in high risk for DS, an amniocentesis should be performed. PSMSUM's screening efficiency has significantly improved with the first- and second-trimester combined tests, with a detection rate of 90–95% and a false positive rate of 2–5% (Tu et al., 2016). According to this study, STQS outperformed both STDS and STTS.

3.1. Various screening methods

Since the 1980s, prenatal screening with maternal serum and ultrasound markers (PSMSUM) have been useful methods for reducing the Foetal complications. Tu et al., (2016) observe that, in contrary to international guidelines, prenatal detection in China has typically depended on invasive maternal age-based testing (Li et al., 2016). The second-trimester triple test [alphafetoprotein (α-FP), human chorionic gonadotrophin (hCG) or free b-hCG, and unconjugated oestriol (uE3)] is the most used screening test, with only a few centres in large cities able to offer alternative screening tests such as the first trimester combined test or the cell-free foetal DNA (cffDNA) blood test. (Li et al., 2016).

Nuchal translucency thickness (NT), an ultrasonographic marker discovered in the 1990s, may differentiate roughly 75% of foetuses with Down syndrome early in the pregnancy when combined with maternal age. The researchers discovered that using NT testing in conjunction with assessing levels of pregnancy-associated plasma protein A and free β-hCG in the first trimester resulted in an 83% detection rate (DR) and a 5% false positive rate (FPR) (Wang et al., 2006).

Even though there is a more reliable cell-free foetal DNA test, the quadruple test is still used for foetal Down syndrome screening, particularly for developing countries, due to its high cost (Pranpanus et al., 2021). Many investigations in developing countries have validated the screening effectiveness of this test, with a satisfactory detection rate for Down syndrome screening. Using an ethnic-specific reference range has a significant influence on diagnostic performance in each population, according to this research and data from earlier studies (Pranpanus et al., 2021). In all cases of defective chromosomes or where a genetic condition was suspected, baby karyotyping was done (Wang et al., 2006).

According to Du, et al. (2017), the clinical value of a second trimester ultrasound screening of foetal nasal bone development in identifying chromosomal abnormalities is significant. In pre-screened populations, the absence of foetal nasal bone is a highly specific ultrasonographic diagnostic for identifying chromosomal disorders.

Moreover, in the first or early second trimester, incremental use of serological screening, ultrasound screening, and non-invasive DNA testing can determine if the foetal nasal bone is still a useful ultrasound soft marker in detecting chromosomal abnormalities (Du et al., 2017). Pregnant women above the age of 35 or those found to be at high risk by the screening test were given advice on invasive prenatal diagnostic procedures. In addition to foetal nasal bone length, recent studies have shown that prenasal thickness and the prenasal thickness-to-nasal bone length ratio may be performed as efficient soft ultrasonography indicators for Down syndrome screening (Du et al., 2017).

A study by Chuanlin Li, et al. (2016) in Hospital of Kunming Medical University reported that there are two categorisation of screening tests performed during first trimester combined screening, which are pregnancies screened with 'low risk' and 'high risk'. Cytogenetic tests revealed 22 chromosomal abnormalities in foetuses that underwent karyotyping, including foetuses with trisomy 21, trisomy 18, Turner syndrome, and other chromosomal abnormalities. Prior to delivery, ultrasonography revealed severe structural and cardiac abnormalities in trisomy 21 foetuses in a dizygotic twin pregnancy (Li et al., 2016). By sequencing cell-free DNA in maternal plasma, pregnant women with assisted reproductive techniques (ART) twin pregnancies were prospectively evaluated by NIPT for trisomy 21 (T21), 18 (T18), and 13 (T13). Positive NIPT results were verified with karyotyping, whereas negative results were followed up on after delivery with an interview. During post-test counselling, the pregnant option based on non-invasive prenatal testing (NIPT) and confirmation results was addressed (Tan et al., 2016). Amniocentesis was conducted after NIPT positive results, followed by karyotyping and, if necessary, the therapy of multifetal pregnancy reduction (MFPR). Standard healthcare interventions were offered for NIPT negative results.

Maternal Serum Screening (MSS) is suggested as an alternative to amniocentesis by doctors. It said that, in contrast to invasive prenatal diagnostic tests, MSS is both safe and inexpensive, making it more acceptable to pregnant women and allowing it to be used more broadly. It marketed MSS as "minimal risk and extremely effective" for DS and neural tube defects (NTD) (Zhu, 2013).

In research by Wanapirak et al. (2012), The DefiaXpress system (Perkin Elmer, Waltham, MA, USA) was used to quantify maternal serum AFP. To reduce variability within tests, all assays and results were done in batches. Using a standardised protocol, information on maternal body weight, gravidity and parity, ethnic origin, and smoking habits was always obtained at the time of blood sample collection. Depending on Caucasian gestation-specific medians and weight correction, blood levels of AFP were converted to multiples of median (MoMs). The computerised machine completed this step automatically. Based on the combination of maternal age and gestational age, the adjusted risk of Down syndrome was computed. A positive result was defined as an adjusted risk of 1:250 or above, and karyotyping would be provided.

3.2. Shortcomings of the current screening methods

Most of the literature on this topic is found in China rather than other Asian countries. Chuanlin Li, et al., 2015) note that, technical expertise and cost coverage are the two significant resource limitations for the advent of a first-trimester screening programme in China. To continue conducting scans, all sonographers must be accredited by the Fetal Medicine Foundation (FMF) and recertified by the FMF every year.

In the 1990s, China implemented maternal serum screening programmes since the ultrasonographic examination of NT can only be performed by specially qualified physicians due to the complexity of the test (Wang et al,. 2006). Even though maternal serum quadruple screening detection rates of 75 to 85 percent have been disclosed, these studies also found false positive screening rates ranging from 5 to 14 percent, which can result in elevated numbers of invasive procedures and elevated laboratory costs for karyotyping, both of which are bothersome for low-resource countries.

The ethnic factor is one of the causes for the high false positive rates. Much research has found that integrating the amiss ethnic factor with various serum marker reference ranges results in a larger percentage of false positives (Prapanus et al., 2021). Furthermore, there is insufficient data on the effectiveness and false positive rate of the quadruple test in the Thai population, where the National Thai Health Policy has designated it as the universal Down syndrome screening test for Thai pregnant women. If the automated Western European descent factor (WF) values have an influence on detection or false positive rates, it would raise the cost of new-born care for Down syndrome and increase the rate of invasive procedures, which will contribute to the country's already large national health care budget (Prapanus et al., 2021).

According to Prapanus et al. (2021), there are a lack of facilities and funding in developing countries, as well as a general inability to afford the more expensive cell-free foetal DNA test. Research suggests that the prenasal thickness-to-nasal bone length ratio is not a particularly strong ultrasonography measure for Down syndrome screening in the Chinese population (Du et al., 2017).

According to Li et al., 2016, the predicted performance rates have not been obtained in China, according to local experience with second-trimester screening. The continuous use of biochemistry adjustment models adopted from Western populations, as well as the use of low/high risk thresholds that are not based on the age distribution of Chinese women, are among the causes for this. Even after adjusting for weight and ethnicity, reported AFP and free b-hCG multiples of the normal median (MoMs) were 11–26% and 30–45% higher than predicted, respectively (Li et al., 2016).

In mainland China, most of foetal ultrasound scans are usually conducted by radiologists rather than obstetricians or maternal foetal medicine experts, which is a divergence from standard practise (Li et al., 2016). Despite its vast geographical and population size, mainland China currently has less than 80 sonographers listed on the FMF website as having a certificate of competence in nuchal translucency (NT) measuring. Despite multiple studies confirming its advantages, most of contemporary sonographers doing first-trimester NT assessments are unaccredited and not subject to external quality assurance evaluation (Li et al., 2016). Moreover, in a study by Miao et al. (2012), stated that the level of knowledge in NT thickness evaluation may not have been adequate, resulting in lower accuracy of first trimester and integrated screening findings. The assessments made by the rather inexperienced personnel might be less accurate than those made by novice personnel using a procedure that is not even widely established.

4. Analysing screening methods of foetal abnormalities associated with AFP

This section mainly discussed the screening methods of foetal abnormalities associated with abnormal AFP level. During the development of the baby, some Alpha-

Fetoprotein **(**AFP) passes through the placenta and enters the mother's circulation. An AFP test is used to evaluate a pregnant woman's AFP levels throughout the second trimester of the pregnancy. A birth defect or other issues may be indicated by a high or low amount of AFP in a mother's blood. According to the recent studies, the serum levels of AFP in Down Syndrome (DS) foetuses were lower than in normal foetuses, and levels are greater in patients who had a lower body weight. AFP levels are anticipated to increase with advanced pregnancy after roughly 17 weeks. (Pranpanus et al., 2021)

Further testing is required to ascertain the level of risk because elevated or decreased levels of AFP in the mother point to a high likelihood of birth defects. There is an increased chance of obstetric issues such as premature membrane rupture, placenta accreta, increta, and percreta even though many women with high maternal AFP do not experience birth defects (Dayal & Hong, 2022). Patients with a lower maternal body weight had greater serum AFP values, per recent studies. As gestational age advances through the first trimester, AFP concentrations typically increase; however, it decreases as maternal weight increases. This confirms that maternal weight-adjusted for multiples of the median (MoM) has an impact on maternal serum levels. The maternal weight adjustment for serum calculation is therefore very important. Recent research has also shown that race and ethnicity significantly affect blood concentrations in both Down syndrome (DS) and normal foetuses during gestation. Maternal serum quadruple indicators do not have globally defined limits for screening for Down syndrome in all races and ethnicities, according to other research that has found differences in normative median serum levels in subgroups of the same nations or ethnicities. Mothers who gave birth to DS children were much older than women who gave birth to non-DS children, according to Miao et al. (2012). Women who gave birth to children with DS had significantly lower AFP MoM levels than mothers who gave birth to children without DS.

Down syndrome may be caused by low AFP levels. The maternal should maintain body weight by leading a healthy lifestyle and consuming a balanced diet. As mentioned previously, the levels of AFP heavily depend on the maternal body weight. To maintain a healthy body weight throughout the pregnancy, family members like the husband and medical professionals should examine the mother's weight at least once each week.

4.1. Screening of AFP in developing countries

The implementation of low-cost screening strategies, such as Hong Kong first-trimester screening models, is necessary to lower the cost of the tests since foetal abnormalities, but such diagnose methods are difficult to apply in underdeveloped nations. Additionally, this method is effective and can provide other benefits (Li et al., 2016). Second-trimester double screening (STDS) and second-trimester triple screening (STTS) were the PSMSUMs the most frequently used by Chinese women, according to Tu et al. (2016). Their exceptional stated screening performance can produce appropriate results in medium- and low-income countries. Due to its higher cost than STDS or STTS, second-trimester quadruple screening (STQS) was hardly used. In China, STQS costs twice as much as STDS since the inhibin-A reagent must be imported (Tu et al., 2016). Compared to first-trimester methods, PSMSUM testing in the second trimester is more economical and technically viable. They are more suited for locations with fewer resources, whereas the first-trimester PSMSUM is better for areas with

plenty of resources. Furthermore, Chen et al. (2007) found that a maternal serum screening strategy may be cost-effective if the uptake rate of chorionic villus sampling (CVS) or AC for patients with positive blood testing increases while the cost of serum screening decreases. The robustness of the maternal age screening approach is impacted by the prevalence of DS in pregnant women 35 years of age and older as well as the expense of prenatal diagnosis. If the rate of prenatal diagnosis increased in women who had been positively screened as well as in women 35 years of age and older, the incremental cost-effectiveness ratio would decrease. Most research suggest that serum screening is more effective and economical than age screening.

4.2. Screening for varied races and ethnicities

The researchers must take an active role in creating global screening standards for Down syndrome in maternal of all races and ethnicities since maternal serum quadruple markers now do not have universally agreed thresholds (Pranpanus et al., 2021). In a study by Wanapirak et al. (2012), Thai models were used instead of computed Caucasian models, resulting in a false-positive rate that was reduced from 10% to 7.1% and weight-adjusted gestation-specific medians that may have prevented a lot of unnecessary prenatal testing. The Caucasian reference range produces a positive rate that is far higher than it ought to be even after weight correction, demonstrating the necessity for ethnicity-specific medians (Praikaew, 2021). Serum concentrations of all these markers were found to be significantly greater in Asian pregnant women, even after adjusting for body weight. Because a simple weight change might not lessen the impact of the ethnic element, each ethnic group should have its own set of reference markers (Wanapirak et al., 2012). The distinct Asian communities, whether from East, South, or Southeast Asia, should have their own databases to be more precise (Wang et al., 2006).

4.3. Diagnosis in high-risk birth

This viewpoint frames potentiality in terms of worry over a rise in the number of babies born with abnormalities and serious problems, a problem that can only be resolved by maternal-health education programmes, maternal serum screening (MSS) testing, amniocentesis, and abortions. Prenatal screening tests that are advised can accurately forecast a woman's risk of carrying a deformed foetus and aid in preventing "imperfect" births, enhancing the quality of the child who will be born and the population of the nation in the future (Zhu, 2013). Children with birth defects can also be born to low-risk mothers. For a precise diagnosis, an amniocentesis should be performed. An amniocentesis should be carried out if the mother is in a high-risk situation. With the first and second trimester combined tests, PSMSUM's screening effectiveness has greatly increased, with a detection rate of 90-95% and a false positive rate of 2-5%. (Tu et al., 2016). This study found that STQS performed better than STDS and STTS.

4.4. Effective screening technique

The MSS test simply takes a tiny sample of blood from a pregnant woman; there is no risk of miscarriage and no harm is done to the foetus. The state was able to check every foetus (and hence every pregnant woman) for potential defects because of the test's safety and promotion as such. Doctors advised amniocentesis for everyone who had a positive MSS test, not only those over 35 or with a family history (Zhu, 2013). Prospective parents were more likely to choose the MSS test when comparing the risk of having a genetically abnormal child against the expense, ease, and safety of the

test as a precaution to avoid being the "one" who had an unhealthy child. Wan et al. (2006) found that triple screening performed better than double screening in the second trimester. Compared to age screening followed by a diagnosis technique, serum screening comes with a higher level of safety. Additionally, serum screening finds more cases of DS than age screening does. Because of this, even though the serum procedure is safer and more efficient, it still requires more resources to produce better outcomes (Chen et al., 2007).

According to Miao et al. (2012), integrated screening was the best way to identify Down's syndrome in a Chinese population. Prenatal DS screening takes into account the maternal age, the timing (first trimester, second trimester, or integrated), and the signs looked at. In the first trimester, ultrasound is frequently used to measure the nuchal translucency (NT) thickness, maternal serum-free beta-human chorionic gonadotrophin (β-hCG), and pregnancy-associated protein-A (PAPP-A) concentrations. Second trimester DS screening in some nations, like China, often include measuring the amounts of maternal serum β-hCG, alphafetoprotein (AFP), unconjugated oestriol (triple screening), and inhibin A (quadruple screening), or b-hCG and AFP concentrations (double screening). In an integrated screening, measures are taken throughout both the first and second trimesters, after which the likelihood of Down syndrome is calculated. According to Wang et al (2006)'s research, the triple-screening method performs better than the second-screening strategy.

4.5. Biochemical screening in (ART)

Ultrasonography is the most often utilised screening method because the usefulness of biochemical screening in Assisted Reproductive Technology **(**ART) twin pregnancies is still uncertain. As a result, a reliable prenatal screening technique is essential for ART twin pregnancies. Prenatal screening in ART pregnancies is now done using noninvasive prenatal testing (NIPT), which analyses cell-free DNA in maternal blood in circulation (Tan et al., 2016). In multiple earlier studies, it was discovered that NIPT has good specificity and sensitivity for detecting common foetal aneuploidies in singleton pregnancies. Tan et al. (2016) looked into how NIPT was included in the typical ART therapy workflow at a single IVF centre and how the findings were used to affect pregnant women's decisions and improve pregnancy outcomes. A positive NIPT result in an ART twin pregnancy can be used as a trustworthy marker for additional prenatal diagnosis (Tan et al., 2016). Prenatal screening with NIPT in ART twin pregnancies would primarily benefit from early and accurate screening results, as well as reduce the challenges associated with determining pregnancy. According to Tan et al. (2016), NIPT may be performed early in pregnancy and has a very low FPR and a very high PPV. It, therefore, has the potential to increase the detection of affected foetuses while decreasing the danger of unnecessary invasive operations.

4.6. The experts' role for healthy birth

The experts ought to view themselves as "quality inspectors" whose job it is to guarantee a healthy birth by urging each expectant mother to take proactive measures to do so. The idea of preventing a "threat" to quality before it arises, or before it becomes reality, must be put into practice (being born). Women should be successfully included in the state's interests in a market-driven economic change, and public education should be used to raise population quality overall (Zhu, 2013). Pregnant women should attend public education programmes before going to the clinic so that they are fully informed about prenatal care. Public school

classes each have their own goals. Their main goal is to ensure that every woman is enrolled in the state perinatal healthcare system in order to raise the standard of care for all newborns (Zhu, 2013). In public education classes, expectant mothers were informed that while the chances of having a child with Down syndrome is one in 1,000, if they are that one chance, then the risk is 100% for them. As a result, the expectant mother should perform as many tests as she can in order to identify a damaged foetus as soon as feasible (Zhu, 2013). Evidence suggests that a lack of knowledge and awareness of screening options is to blame for China's low acceptance of DS screening. Consequently, suggestions on how to give women adequate and timely screening information should be developed (Tu et al., 2016). Professional genetic counselling can help patients understand the significance and advantages of additional testing and reduce the potential of bad advice, resulting in improved diagnosis uptake (Chen et al., 2007).

4.8. Maternal Serum Screening (MSS) policy

Serological screening should be done in situations where the NT thickness evaluation's accuracy cannot be ensured; both for test validity and financial reasons (Miao et al., 2012). It is necessary to develop MSS delivery policy strategies. In numerous nations, it has been demonstrated that an integrated delivery strategy focused on primary healthcare is effective and efficient in providing MSS and other diagnostic tests. Prior to this, MSS was only accessible in China through specialised medical centres or prenatal diagnostic facilities (Li et al., 2015). Service networks are constrained, requiring a change in policy. The reform of MSS delivery should lessen regional disparities in the MSS uptake rate as long as primary healthcare is of adequate quality and its function is acknowledged.

The overall fault rate will be lower if it can identify problems before the product (baby) is done. It is strongly encouraged to get every medical exam possible, including prenatal tests. Following the recommendations for prenatal medical exams will surely help in accomplishing a similar goal and will raise the product's quality at the least expensive rate (Zhu, 2013). Marketing for prenatal testing promoted it as a cost-effective investment that would result in savings down the road.

According to Zhu (2013), stress at work can affect pregnant women emotionally, which can directly affect the foetus. Smoking and drinking were seen to be examples of "bad" habits that could harm an unborn child. Nowadays, women prioritise their careers over getting married. To avoid interfering with their work, they postponed getting married and starting a family. When they finally decide to start a family, it is either too late or causes a plethora of problems, such as infertility, spontaneous abortions, and a high likelihood of having a child with a deformity (Zhu, 2013).

4.9. Role of the govern in technology used for foetal abnormalities screening

The kit can detect DS, 18 trisomy, 13 trisomy, as well as other chromosomal abnormalities and NTD diseases using only two biomarkers, according to Beijing Worldson Biological Technology, which imports the kit from Genemed Biotechnologies. The kit's comprehensive nature also eliminates the need for other specialised and expensive tests. The kit is claimed to be pertinent to both Chinese and other Asian countries since many Chinese people believe that different races have biological peculiarities (Zhu, 2013).

The market for prenatal screening test kits will grow as a result of the family planning committees and the health ministry's defective birth intervention

programme. The government's yousheng (eugenics or healthy birth) activities have a significant impact on the market for prenatal healthcare products in China (Zhu, 2013). To boost the national screening plan, quality assurance programmes and an ongoing evidence base must be developed with a steady resource stream, knowledgeable leadership, and good clinic-laboratory collaboration (Tu et al., 2016).

To achieve the best screening results, national rules on technical standards, resource allocation, and quality assurance must be made public and promoted. For instance, the majority of European countries advocate early screening and first-trimester combined screening. In the United Kingdom and Canada, minimum performance criteria are suggested, whereas national standards in the United States place an emphasis on the appropriateness of screening processes in light of the context and available resources. In addition to national guidelines, ongoing quality control programmes and an evidence base that is continuously updated must be built. Both of these initiatives must be backed by a resource stream (Tu et al., 2016). A nationwide prenatal ultrasound testing guideline recommends that the prenatal ultrasound test be standardised and that practitioners be accredited. To ensure that everyone has equal access to MSS, especially in Asian countries, the entire structure of MSS service delivery should be assessed during policy formulation (Li et al., 2015). A national regulation for the administration of prenatal diagnosis procedures was published by the Chinese Ministry of Health (MOH) in 2003 with the intention of enabling prospective parents to identify and manage their risk of birth defects, make educated reproductive decisions, and increase the safety of deliveries. Setting a fair price is essential since it affects incentives (Chen et al., 2007). In order to reach a suitable price ratio, the healthcare administration and pricing authority should base the price of health services on unit costs. According to Chen et al. (2007), the government should increase the cost of prenatal diagnostic services while decreasing the cost of serum screening tests to provide a reasonable inducement for the supplier. If the cost of the serum screening test was reduced, prenatal testing for Down's syndrome would be easier for pregnant women in rural and metropolitan areas.

5. Conclusion

The Islamic teachings and scientific research have emphasized on importance of healthy generations for better life on earth. Muslim jurists have concluded that perseveration of ‘Progeny’ is among the five final objectives of Islamic law (Shari`ah), because the Holy Qur`an has emphasized in many verses the importance of reproductivity and giving care to new generations. Applying the scoping review approach, this article has analyzed the screening methods on foetal abnormalities associated with AFP levels. The main purpose of the study is to provide a holistic view on screening method. This approach comprises various analytical aspects, including data analysis and evaluation of the screening methods. This comprehensive research strategy included a number of analytical components, such as a conceptual framework, data analysis, thorough examination, and evaluation of the diagnostic and screening techniques. The scoping review technique is used to determine the research progress on this topic and to identify the relevant works on screening methods AFP level and to recognise multidirectional cause and effect interactions within the health care system, which is a complex web of interdependencies.

The study has concluded that the effective screening methods, systematic guidelines, standards and government

regulations that aim to ensure the health of maternal and neonatal populations should be adopted in order to reduce foetal anomalies and improve the quality of the newborn population. Due to the fact that the systematic application of screening method for detection foetal defects in developing nations might be challenging, because some screening techniques are expensive, it is recommended that first-trimester screening models be utilised instead. Potentially, maternal health education, early MSS testing, and amniocentesis are the most efficient ways to reduce the rising number of infants born with abnormalities and serious problems. Prenatal screening tests can effectively forecast a woman's likelihood of carrying a malformed foetus and help prevent "imperfect" births, improving the quality of the future child for the family and the nation's population.

The integrated screening was the most effective method for identifying prenatal abnormalities in Asian nations. Integrated screening entails assessing the risk of foetal abnormalities throughout both the first and second trimesters. By establishing reproduction technologies to track and manage family reproduction as well as high-risk pregnancies, the health authorities of these nations must play a crucial role in lowering congenital abnormalities. This allows for the monitoring of medical care during pregnancy, including prenatal developments, labour and delivery, and postpartum follow-up. It is also important to provide comprehensive care for women before, during, and after pregnancy and childbirth. By guaranteeing the health of expectant mothers and babies, healthy future generations will be produced.

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