

Correlation Between Prematurity and Abnormal Hearing-Screening Outcomes in a Tertiary Pediatric Population: A Retrospective Study

Fani Paulina^{1*}, Devy Kusmira², Depi Jufri³

¹Department of Ear, Nose, Throat, Head and Neck Surgery, Faculty of Medicine, Universitas Indo Global Mandiri, Palembang, Indonesia

²Faculty of Medicine, Universitas Indo Global Mandiri, Palembang, Indonesia

³Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

*E-mail: fani.paulina@email.com

Abstract

Prematurity is a recognized risk factor for neonatal hearing impairment, but its independent contribution may be difficult to distinguish from coexisting neonatal morbidities and intensive-care exposures. This study aims to assess the association between prematurity and abnormal hearing-screening outcomes and to describe the distribution of abnormal outcomes according to selected perinatal risk factors. This retrospective observational study included 349 participants who underwent otoacoustic emissions and/or auditory brainstem response testing. Participants were classified according to gestational age at birth as preterm (<37 completed weeks) or term (≥37 completed weeks). An abnormal outcome was defined as a “refer” result in either ear on either test. Groups were compared using the chi-square test and odds ratio (OR). Of 349 participants, 240 (68.8%) were born preterm and 109 (31.2%) were born at term. Overall, 169 participants (48.4%) had an abnormal hearing-screening result. The proportion was 45.8% (110/240) among premature participants and 54.1% (59/109) among term participants, with no significant difference ($\chi^2=1.746$; $p=0.186$; $OR=0.72$, 95% CI 0.45–1.13). High proportions of abnormal screening outcomes were observed among participants with documented ototoxic drug exposure (13/13, 100%), asphyxia (27/36, 75.0%), and hyperbilirubinemia (13/19, 68.4%). Prematurity alone was not associated with abnormal early hearing-screening outcomes in this high-risk population. The high referral rate supports universal screening and targeted audiological follow-up, particularly for participants with ototoxic exposure, asphyxia, or hyperbilirubinemia.

Keywords: Prematurity, Neonatal Hearing Screening, Otoacoustic Emissions, Auditory Brainstem Response, Hearing Loss

1. Introduction

Permanent hearing loss is among the most common congenital sensory disorders and may substantially affect a child’s communication and development. A systematic review and meta-analysis of universal newborn hearing screening programs estimated the pooled prevalence of permanent childhood hearing loss detected at birth to be approximately 1.1 per 1,000 screened participants, with a nearly sevenfold higher prevalence among those admitted to neonatal intensive care units (NICUs).^{1–3} In Indonesia, nationally representative data on congenital hearing loss remain limited because newborn hearing screening is not uniformly implemented; a 2024 review

reported prevalence estimates of approximately 0.08% in 2013 and 0.11% in 2018, while also emphasizing that the national epidemiology is fragmented and based largely on single-site or multicenter studies. Because adequate auditory input during early life is essential for speech and language acquisition, delayed identification and intervention may result in persistent developmental, educational, and psychosocial consequences. Universal newborn hearing screening (UNHS), using otoacoustic emissions (OAE), automated auditory brainstem response (AABR), or a combination of these methods, facilitates early identification and timely access to diagnostic evaluation and intervention. Evidence indicates that children

identified through UNHS receive amplification and early intervention at younger ages and generally achieve better language and literacy outcomes than those identified later.^{4,5}

Preterm birth, defined as delivery before 37 completed weeks of gestation, is a risk factor for childhood sensorineural hearing impairment. Importantly, the risk appears to increase with decreasing gestational age. In a recent Norwegian population-based cohort, sensorineural hearing impairment occurred in 1.4% of preterm-born children compared with 0.7% of term-born children. Compared with children born at term, the adjusted risk was 1.7-fold higher among those born moderate-to-late preterm, 3.3-fold higher among those born very preterm, and 7.6-fold higher among those born extremely preterm. Large neonatal screening databases have similarly demonstrated that premature participants have a higher prevalence of abnormal screening results and confirmed hearing impairment, particularly at lower gestational ages and birth weights.^{6,7}

Nevertheless, the relationship between prematurity and hearing impairment is complex and cannot necessarily be attributed to gestational age alone. Premature participants frequently experience multiple neonatal morbidities and require prolonged intensive care. Consequently, they may be exposed to mechanical ventilation, oxygen therapy, hypoxic-ischemic events, severe hyperbilirubinemia, sepsis, and potentially ototoxic medications such as aminoglycosides.^{1,6} These exposures may affect the cochlea, auditory nerve, and central auditory pathways, either independently or synergistically. The clustering of these factors also makes it difficult to distinguish the independent effect of prematurity from the effects of neonatal illness and its treatment. Furthermore, an initial “refer” result on OAE or AABR indicates the need for additional audiological assessment and should not be

considered equivalent to a confirmed permanent hearing-loss diagnosis.^{8,9}

Although the association between prematurity and hearing loss has been investigated in several large cohorts, most available evidence originates from high-income countries with established newborn hearing-screening systems. Screening coverage, referral pathways, follow-up completion, and the distribution of neonatal risk factors may differ considerably in resource-limited settings. Local evidence is therefore needed to support context-specific screening and audiological follow-up strategies.¹⁰ Accordingly, this study aimed to evaluate the association between preterm birth and abnormal OAE and/or ABR outcomes among pediatric patients undergoing hearing assessment at a tertiary referral center and to describe the distribution of abnormal screening outcomes according to selected perinatal risk factors.

2. Method

2.1. Study Design and Setting

This retrospective analytical cross-sectional study was conducted using secondary data obtained from pediatric medical records at the Otorhinolaryngology–Head and Neck Surgery outpatient clinic of Dr. Mohammad Hoesin Hospital, Palembang, Indonesia. The study protocol was approved by the Health Research Ethics Committee of Dr. Mohammad Hoesin Hospital, Palembang, Indonesia (No. 06/KEPKRSMH/2021). Patient information obtained from medical records was handled confidentially and used solely for research purposes. Medical records from patients evaluated between January 2019 and February 2021 were reviewed to examine the association between prematurity and abnormal hearing-screening outcomes, as well as the distribution of other recognized risk factors for congenital or early-onset hearing loss.

2.2. Sample Size Determination

Because this retrospective study used secondary medical-record data, all eligible records available during the predefined study period from January 2019 to February 2021 were included using a total-sampling approach. Therefore, no a priori sample-size calculation or specific sample-size formula was applied. The final sample size was determined by the number of records fulfilling the eligibility criteria, resulting in 349 participants. Because a contemporaneous screening log was unavailable, the total number of records initially assessed and subsequently excluded could not be reconstructed.

2.3. Study Participants

The study population comprised pediatric patients who underwent otoacoustic emissions (OAE) and auditory brainstem response (ABR) examinations during the study period. Records were eligible for inclusion when the patient had an intact tympanic membrane, a type A tympanogram, documented OAE and ABR findings, and sufficient demographic and clinical information for analysis. Only records with available information on gestational age or prematurity status were included in the analysis of the association between prematurity and hearing-screening outcomes.

2.4. Data Collection and Study Variables

The data were extracted from the hospital medical record system using a standardized data collection form. The demographic and perinatal variables collected included age at the time of hearing examination, sex, and mode of delivery.

Information regarding potential risk factors for congenital or early-onset hearing loss was also recorded. These factors included: a family history of congenital hearing loss, syndromes known to be

associated with sensorineural hearing loss, maternal TORCH infection or syphilis during pregnancy, maternal exposure to potentially ototoxic medications during pregnancy, prematurity, low birth weight, perinatal asphyxia, and hyperbilirubinemia. Prematurity was defined as birth before 37 completed weeks of gestation. Accordingly, patients were categorized as: preterm (gestational age <37 weeks) or term (gestational age ≥37 weeks). Although clinically meaningful strata include extremely preterm (<28 weeks), very preterm (28 to <32 weeks), and moderate-to-late preterm (32 to <37 weeks), complete gestational-age data were not consistently available for all eligible records; therefore, severity-stratified analyses were not performed.

2.5. Hearing Assessment and Outcome Definition

Auditory function was evaluated bilaterally using OAE and ABR. OAE testing was used to assess cochlear outer hair-cell function, whereas ABR was used to evaluate neural conduction along the auditory pathway from the cochlea and eighth cranial nerve to the brainstem. The result for each ear was classified as either “pass” or “refer.” A “pass” result indicated that the screening criteria were met, whereas a “refer” result indicated that further audiological assessment was required. For the present analysis, the primary outcome was an abnormal hearing-screening result, defined as a “refer” finding in at least one ear on OAE and/or ABR. Because a screening referral does not necessarily represent permanent sensorineural hearing loss, these findings were not interpreted as a definitive diagnosis of hearing impairment.

2.6. Statistical Analysis

Statistical analyses were performed using SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). Categorical variables were

summarized as frequencies and percentages, whereas continuous variables were presented as medians and ranges. The proportion of abnormal hearing-screening outcomes was compared between preterm and term patients using the chi-square test. The magnitude of the association was expressed as an odds ratio (OR) with a 95% confidence interval (CI). The distribution of age between patients with “pass” and “refer” results was compared using the Mann–Whitney U test. Multivariable logistic regression was not performed because several covariates had incomplete documentation and sparse cells, particularly for individual neonatal risk factors and gestational-age strata; a multivariable model would therefore have produced unstable estimates and could have been overfitted. The analysis was consequently limited to univariable descriptive and bivariate tests. All statistical tests were two-sided, and a p-value of <0.05 was considered statistically significant.

3. Result

3.1. Participant Characteristics

A total of 349 pediatric patients met the eligibility criteria and were included in the analysis. The retrospective database was not accompanied by a contemporaneous screening log; consequently, the initial number of records assessed before inclusion/exclusion and the exact number excluded for each criterion could not be reconstructed. The final cohort comprised all available records that met the predefined criteria. Records were excluded from the analytic dataset when the tympanic membrane was not intact, tympanometry was not type A, OAE and/or ABR findings were unavailable, demographic or clinical information was insufficient, or gestational-age/prematurity information was missing for the prematurity analysis.

The median age at the time of hearing assessment was 30 weeks, with a range of 3–195 weeks. Because this study was conducted in a tertiary otorhinolaryngology referral setting, hearing assessments were performed across a wide age range. The retrospective medical records did not consistently indicate whether each examination represented initial screening, rescreening, or subsequent audiological evaluation. Patients were retained in the analysis when they fulfilled the predefined eligibility criteria. The wide age range should therefore be considered when interpreting and generalizing the findings. Based on gestational age at birth, 240 patients (68.8%) were born preterm, whereas 109 (31.2%) were born at term. Thus, more than two-thirds of the study population consisted of children with a history of prematurity (Table 1).

3.2. Hearing-Screening Outcomes

Of the 349 patients evaluated using OAE and ABR, 180 (51.6%) achieved a “pass” result, whereas 169 (48.4%) had a “refer” result in at least one ear on one or both screening modalities (Figure 1).

According to the predefined study outcome, these 169 patients were categorized as having an abnormal hearing-screening outcome. However, a “refer” result indicated the need for further audiological evaluation and was not considered equivalent to a confirmed diagnosis of permanent hearing loss.

3.3. Association Between Prematurity and Hearing-Screening Outcomes

Among the 240 preterm patients, 110 (45.8%) had an abnormal hearing-screening result, compared with 59 of the 109 term patients (54.1%). The proportion of abnormal screening outcomes was therefore numerically lower in the preterm group than in the term group.

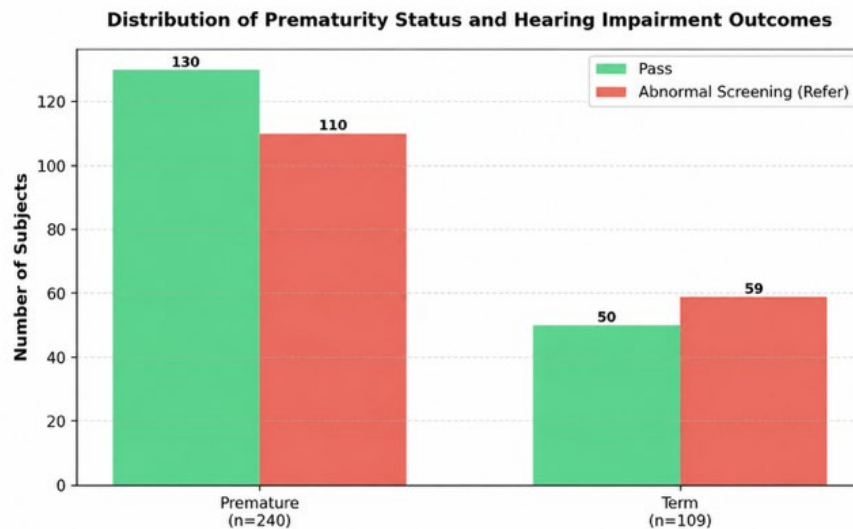


Figure 1. Distribution of Prematurity Status and Hearing-Screening Outcomes

However, the difference between the two groups was not statistically significant ($\chi^2=1.746$; $p=0.186$). Preterm birth was associated with an odds ratio of 0.72 for an abnormal hearing-screening result compared with term birth; however, the 95% confidence interval included the null value (95% CI 0.45–1.13). Therefore, prematurity was not significantly associated with an increased likelihood of an abnormal hearing-screening outcome in this study population (Table 2).

3. 4. Hearing-Screening Outcomes According to Associated Risk Factors

Among the risk factors with available documentation, the highest proportion of abnormal hearing-screening outcomes was observed in patients with a history of ototoxic

drug exposure. All 13 patients with documented ototoxic exposure had a “refer” result, corresponding to a proportion of 100%. In comparison, 46.6% of patients without documented ototoxic exposure had an abnormal screening result.

Abnormal hearing-screening outcomes were also identified in 27 of 36 patients with a history of asphyxia, corresponding to a proportion of 75.0%. Among patients without a documented history of asphyxia, the proportion was 45.4%. Similarly, 13 of 19 patients with hyperbilirubinemia had an abnormal hearing-screening result, corresponding to a proportion of 68.4%, compared with 47.3% among patients without documented hyperbilirubinemia (Table 3).

Table 1. Baseline Characteristics of The Study Population

Characteristic	Value
Age at hearing assessment, median (range), weeks	30 (3–195)
Male, n (%)	230 (65.9)
Female, n (%)	119 (34.1)
Preterm birth, n (%)	240 (68.8)
Term birth, n (%)	109 (31.2)
Pass, n (%)	180 (51.6)
Refer, n (%)	169 (48.4)

Table 2. Association Between Birth Status and Hearing-Screening Outcomes

Birth Status	Pass (n)	Refer (n)	Total	Proportion with Abnormal Screening Outcome (%)
Term (≥ 37 weeks)	50	59	109	54.1%
Premature (< 37 weeks)	130	110	240	45.8%
Total	180	169	349	48.4%

$\chi^2=1.746$; $p=0.186$, OR=0.72 (95%CI: 0.45–1.13)

Table 3. Abnormal Hearing-Screening Outcomes According To Selected Risk Factors And Documentation Status

Risk-factor status	Total with risk factors, n	Refer, n (%)
Ototoxic drug exposure	13	13 (100%)
Asphyxia	36	27 (75%)
Hyperbilirubinemia	19	13 (68.4%)

4. Discussion

The present study evaluated the association between prematurity and abnormal hearing-screening outcomes among 349 pediatric patients undergoing OAE and ABR assessment. The principal finding was that prematurity, when analyzed as a binary variable, was not significantly associated with an abnormal hearing-screening result. A “refer” outcome was observed in 45.8% of preterm patients and 54.1% of term patients, corresponding to an OR of 0.72 (95% CI, 0.45–1.13; $p=0.186$). In contrast, high proportions of abnormal screening results were observed among patients with documented ototoxic drug exposure, asphyxia, and hyperbilirubinemia. These findings suggest that, within this selected clinical population, hearing-screening outcomes may reflect the combined influence of perinatal and clinical risk factors rather than prematurity alone.

The absence of a significant association between prematurity and abnormal hearing-screening outcomes differs from several large population-based and neonatal cohort studies. In a nationwide Dutch cohort of 18,564 very preterm neonates, the prevalence of neonatal hearing loss increased progressively with decreasing gestational age, from approximately 1.2% at 31 weeks to 7.5% at 24 weeks, and also increased with decreasing birth weight.¹¹ Similarly, a Finnish

national register study involving more than one million children demonstrated an increased risk of hearing loss among both very preterm and late-preterm children compared with those born at term.¹² Data from national newborn hearing-screening programs have also demonstrated a greater burden of abnormal hearing outcomes among premature participants.¹³ Collectively, these findings support prematurity as an important marker of increased auditory risk, particularly at very low gestational ages.

Several factors may explain the discrepancy between these previous findings and the results of the present study. First, the study population was derived from patients who underwent OAE and ABR evaluation at a tertiary otorhinolaryngology service rather than from an unselected birth cohort. Consequently, term-born patients included in the study may not represent healthy term participants in the general population and may instead have been referred because of other clinical risk factors for hearing impairment. Such referral or selection bias could increase the frequency of abnormal results in the term group and attenuate the apparent effect of prematurity. Therefore, the finding that preterm patients had numerically fewer “refer” results should not be interpreted as evidence that prematurity is protective against hearing impairment.

Second, the classification of prematurity as a single category of <37 weeks may have obscured the gestational age-dependent gradient of hearing risk. Extremely preterm, very preterm, and moderate-to-late preterm participants have substantially different neonatal courses and risk profiles. Previous evidence indicates that the risk of hearing loss increases substantially at progressively lower gestational ages.¹¹ Combining all patients born before 37 weeks into one group may therefore dilute an association that is predominantly driven by the most immature participants. Future studies should stratify prematurity according to gestational age categories and simultaneously consider birth weight, particularly very low and extremely low birth weight.

Another important consideration is that the outcome evaluated in this study was a hearing-screening referral, rather than diagnostically confirmed permanent hearing loss. The overall “refer” rate of 48.4% is considerably higher than the prevalence of permanent hearing loss generally reported in neonatal populations and should therefore not be interpreted as the prevalence of permanent auditory impairment. A “refer” result on OAE or ABR may occur for several reasons and requires subsequent audiological evaluation before a definitive diagnosis can be established. Studies of premature and NICU populations have demonstrated that a substantial proportion of participants who fail an initial hearing screen subsequently achieve normal results on repeat or diagnostic testing. Yang et al., for example, reported progressive reductions in screening failure during repeated assessments of NICU participants, with most participants who failed the initial TEOAE ultimately demonstrating normal hearing and speech development.¹⁴ More recent NICU data similarly suggest that some abnormalities requiring retesting may be partially or completely reversible.¹⁵

Auditory maturation may also contribute to changes in hearing-test responses over time, particularly among premature participants. Delayed maturation of auditory brainstem pathways has been described in preterm populations, and electrophysiological thresholds may improve during subsequent follow-up.¹⁴ This issue is particularly relevant to the present study because the age at hearing assessment varied widely, from 3 to 195 weeks. Consequently, patients may have undergone testing at substantially different developmental stages. Furthermore, without information regarding whether each examination represented an initial screening, rescreening, or diagnostic follow-up, the influence of auditory maturation on the observed results cannot be fully determined.

The findings of the present study also emphasize the multifactorial nature of hearing impairment among high-risk participants. Prematurity frequently coexists with low birth weight, respiratory failure, prolonged mechanical ventilation, hypoxic–ischemic events, hyperbilirubinemia, infection, and exposure to potentially ototoxic medications. Therefore, gestational age may function partly as a marker of vulnerability rather than as an isolated causal factor. In a nationwide NICU cohort, Hille et al. found that severe birth asphyxia and assisted ventilation for five days or longer were independent predictors of hearing loss, illustrating the importance of neonatal illness severity and treatment-related exposures.¹⁶ Similarly, studies of NICU populations have identified combinations of prematurity, very low birth weight, hyperbilirubinemia, low Apgar scores, and other perinatal factors as contributors to abnormal hearing outcomes.¹⁵ These observations may help explain why prematurity alone was not associated with screening referral in the present study, particularly when preterm participants were

compared with a potentially high-risk term-born population.

Among the associated risk factors evaluated in this study, all 13 patients with documented ototoxic drug exposure had an abnormal hearing-screening result. Although this finding is notable, it should be interpreted cautiously because of the small number of exposed patients and the absence of adjustment for potential confounding factors. Ototoxic medications, including several antimicrobial agents commonly used in high-risk neonatal care, have been associated with cochlear injury; however, susceptibility may depend on the specific drug, cumulative dose, duration of exposure, concurrent medications, renal function, genetic susceptibility, and underlying severity of illness.⁸ The present dataset did not provide sufficient detail regarding the type, timing, dosage, and duration of ototoxic drug exposure to establish a direct causal relationship. Moreover, because the current analysis was descriptive, the 100% “refer” proportion should not be interpreted as an estimate of the risk attributable to ototoxic exposure.

Perinatal asphyxia was also associated with a high proportion of abnormal screening outcomes, with 75.0% of patients with a documented history of asphyxia receiving a “refer” result. Hypoxic–ischemic injury may affect multiple components of the auditory system, including cochlear and neural pathways. Electrophysiological studies have demonstrated alterations in ABR responses following perinatal asphyxia, supporting the biological plausibility of auditory pathway dysfunction after hypoxic injury.¹⁷ Furthermore, severe birth asphyxia has previously been identified as an independent risk factor for hearing loss in NICU populations.¹⁶ Nevertheless, the present findings remain descriptive, and the absence of data regarding the severity of asphyxia,

Apgar scores, hypoxic–ischemic encephalopathy, and other concurrent neonatal complications limits further interpretation.

Hyperbilirubinemia was another clinically relevant finding, with 68.4% of affected patients demonstrating an abnormal hearing-screening result. The auditory nervous system is particularly vulnerable to bilirubin neurotoxicity, which may predominantly affect the auditory nerve and brainstem auditory pathways and can manifest as auditory neuropathy spectrum disorder.^{18,19} Preterm participants may be particularly susceptible to bilirubin-induced auditory injury because neurotoxicity can occur at lower bilirubin concentrations than in term participants.¹⁸ Previous literature has consistently demonstrated abnormalities in auditory brainstem responses among neonates with significant hyperbilirubinemia, although the bilirubin threshold associated with auditory toxicity remains variable across studies.²⁰ These findings support careful audiological surveillance of children with clinically significant hyperbilirubinemia, particularly when additional neonatal risk factors are present.

Taken together, the present findings reinforce the importance of interpreting hearing-screening results within the broader clinical context. Prematurity remains an established risk marker for hearing impairment, but its impact is likely modified by the degree of prematurity, birth weight, neonatal morbidity, and treatment-related exposures. In high-risk populations, reliance on prematurity status alone may therefore be insufficient to identify children requiring continued audiological surveillance. Participants and children with abnormal initial screening results or relevant perinatal risk factors should undergo appropriate repeat and diagnostic assessment to distinguish

transient or maturational abnormalities from persistent hearing impairment.

This study has several limitations. Its retrospective design made the analysis dependent on the completeness and accuracy of medical records. Data regarding several relevant risk factors were incomplete, preventing a comprehensive multivariable analysis and limiting the ability to determine whether prematurity or other exposures were independently associated with abnormal hearing outcomes. The relatively small number of patients with individual risk factors also resulted in imprecise descriptive estimates. In addition, the study did not consistently distinguish initial screening examinations from repeat or diagnostic assessments and did not include longitudinal confirmatory audiological outcomes. The broad age range at examination may have introduced additional heterogeneity related to auditory maturation. Moreover, defining the outcome as a “refer” result in either ear on OAE and/or ABR may have increased the observed proportion of abnormal results and does not allow differentiation between transient conductive abnormalities, auditory neuropathy, and permanent sensorineural hearing loss. Finally, grouping all preterm patients into a single category may have obscured differences according to the severity of prematurity.

Despite these limitations, this study provides clinical data from a tertiary-care setting and highlights an important distinction between risk factors for abnormal hearing-screening results and risk factors for confirmed permanent hearing loss. The findings indicate that, in this selected population, prematurity alone was not significantly associated with an abnormal OAE and/or ABR result, whereas high proportions of screening referrals were observed among patients with ototoxic drug exposure, asphyxia, and hyperbilirubinemia. Future

prospective studies should incorporate detailed gestational-age categories, birth weight, neonatal intensive-care exposures, standardized timing of hearing assessment, and longitudinal diagnostic follow-up. Multivariable analysis will also be necessary to determine the independent contributions of prematurity and coexisting perinatal risk factors to permanent hearing outcomes.

5. Conclusion

Prematurity was not significantly associated with abnormal hearing-screening outcomes in this study population. However, high proportions of “refer” results were observed among patients with ototoxic drug exposure, asphyxia, and hyperbilirubinemia. These findings highlight the importance of hearing screening and appropriate audiological follow-up, particularly in high-risk participants.

6. Acknowledgment

None.

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