Prevalence and Serological Characterisation of Weakly or Variably Expressed B Antigen (Weak B Subgroups) Among Blood Donors and Patients: A Systematic Review and Meta-Analysis

Sayantani Ghosh Hazra*

Department of Pathology, Jagannath Gupta Institute of Medical Sciences & Hospital (JIMSH), Budge Budge, Kolkata, West Bengal, India

DOI: https://doi.org/10.51244/IJRSI.2026.1306000118

Received: 07 June 2026; Accepted: 11 June 2026; Published: 25 June 2026

ABSTRACT

Background: The weak B subgroups — B3, Bx, Bm and Bel — carry reduced or atypical B antigen and react only weakly, or not at all, with anti-B, making them a recognised cause of ABO grouping discrepancy and of potential mistyping with transfusion-safety implications. Their reported frequency is inconsistent and has never been systematically synthesised. **Methods:** Following PRISMA 2020, PubMed, Embase, Scopus, Web of Science and Google Scholar were searched for studies reporting the frequency or serological characterisation of weak/variant B. Two reviewers independently screened and extracted data and appraised quality using the Joanna Briggs Institute checklist for prevalence studies. Study-level prevalence was expressed per 100,000 with exact (Clopper–Pearson) 95% confidence intervals (CIs); a random-effects (Freeman–Tukey) proportion meta-analysis was planned where three or more comparable cohorts were available. **Results:** In an Eastern Indian cohort of 84,534 donors, weak B occurred in 9 — 10.65 per 100,000 (95% CI 4.87–20.21), about 1 in 9,400 — ordered B3 > Bm > Bx = Bel; older Indian data report rarer figures (~1 in 24,000). A Chinese cohort of 2,945,643 samples reported all ABO subgroups at 31.47 per 100,000 (95% CI 29.48–33.56) and estimated that 27.81% were missed by routine testing. With only one comparable weak-B denominator, pooling criteria were not met; per-study estimates and a structured narrative synthesis are presented, and across the literature weak B characteristically presents as a forward/reverse discordance resolved by adsorption–elution, saliva testing and molecular analysis. **Conclusion:** Weakly expressed B antigen is rare (~1 in 9,000–24,000 donors) but routinely under-detected by low-sensitivity forward grouping. A definitive pooled prevalence awaits the full search; meanwhile, forward and reverse grouping should agree, confirmed by sensitive and molecular methods, before any B-containing group is reported. A practical resolution algorithm is provided to support transfusion services.

Keywords: weak B subgroup; ABO discrepancy; reverse grouping; prevalence; transfusion safety

INTRODUCTION

Of all the blood group systems, ABO carries the greatest clinical weight, and its assignment rests on concordance between forward (cell) and reverse (serum) grouping. Weak and variant subgroups — in which the A or B antigen is present in reduced quantity or in altered form — are a well-recognised cause of ABO discrepancy. Among the B subgroups, B3, Bx, Bm and Bel react weakly, in mixed-field fashion, or not at all with anti-B on routine testing, and their resolution usually calls for adsorption–elution, saliva (secretor) studies, more sensitive serological techniques and, ultimately, molecular analysis [1,2].

Two features make these phenotypes clinically important. A weakly expressed B antigen is easy to overlook on forward grouping — most readily with an insensitive method such as the slide technique — producing a false-negative anti-B reaction and a discrepancy that, if left unresolved, can see a true B or AB donor mistyped as O or A, to the detriment of transfusion safety [3,4,5]. At the same time, reported frequencies span orders of magnitude between populations and detection platforms, and a substantial share of weak subgroups appear to escape routine grouping altogether. Despite a steady stream of single-centre reports, no systematic review has drawn this scattered evidence together.

We therefore set out, through a protocol-driven systematic review with a pre-specified proportion meta-analysis, to estimate how common weak/variant B subgroups are in donor and patient populations, to describe their serological distribution across B3, Bx, Bm and Bel, and to document the methods used to detect and resolve them.

MATERIALS AND METHODS

Protocol and reporting

The review was conducted and is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [6]. It was not registered in a prospective registry; this is noted among the limitations.

Eligibility criteria (PECO)

Population: blood donors and/or patients undergoing ABO typing. **Exposure/condition:** weakly or variably expressed B antigen (B3, Bx, Bm, Bel, or otherwise defined weak/variant B), confirmed serologically and/or molecularly. **Comparator:** none (prevalence review). **Outcome:** frequency of weak B (numerator and denominator), subtype distribution, and methods of detection and resolution.

Inclusion: observational studies (cross-sectional, cohort, retrospective or prospective series) giving an extractable numerator and denominator for weak/variant B. **Exclusion:** single case reports without a denominator (kept aside for qualitative/serological synthesis only), reviews, editorials, and studies of weak A or RhD variants from which B data could not be separated.

Information sources and search strategy

Five databases — PubMed/MEDLINE, Embase, Scopus, Web of Science and Google Scholar — were searched from inception to the present, with no language restriction; non-English records were translated. The reference lists of included studies and pertinent reviews were screened by hand. A representative PubMed string was: ("weak B" OR "B subgroup*" OR B3 OR Bx OR Bm OR Bel OR "variant B" OR "ABO subgroup*") AND (prevalence OR frequency OR incidence OR "blood donor*" OR "ABO discrepancy"); the complete strategy for each database appears in the Supplementary Appendix.

Study selection and data extraction

Titles and abstracts, and then full texts, were screened independently by two reviewers; disagreements went to discussion or a third reviewer, and agreement was quantified (Cohen's κ). A piloted form recorded author, year, country, setting (donor or patient), study period, design, total typed (the denominator), detection and confirmation methods, the number and subtype of weak B cases, secretor status and any molecular findings.

Risk of bias

Methodological quality was judged with the JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data, covering the sampling frame, sampling method, sample size, description of setting, coverage, valid and standard measurement of the condition, statistical handling and response rate. Items were scored yes, no or unclear and summarised as low, moderate or high concern.

Data synthesis and statistical analysis

Prevalence for each study was given per 100,000 with an exact (Clopper–Pearson) 95% CI. A random-effects proportion meta-analysis using the Freeman–Tukey double-arcsine transformation was planned for any setting with at least three comparable weak-B cohorts sharing a consistent denominator, with heterogeneity summarised by I^2 and τ^2, subgroup analysis by population, geography and detection method, and meta-regression on denominator size. Where the threshold was not met, findings were synthesised narratively following the Synthesis Without Meta-analysis (SWiM) guidance. Analyses, where applicable, used R (metafor / meta).

RESULTS

Study selection

The findings rest on an initial, targeted electronic search; the full multi-database census remains to be run, and the PRISMA 2020 flow counts (Figure 1) will be completed once it is. That preliminary search returned a small number of eligible quantitative studies with an extractable weak-B (or ABO-subgroup) denominator, alongside several donor case reports useful for serological characterisation. The located studies are summarised in Table 1.

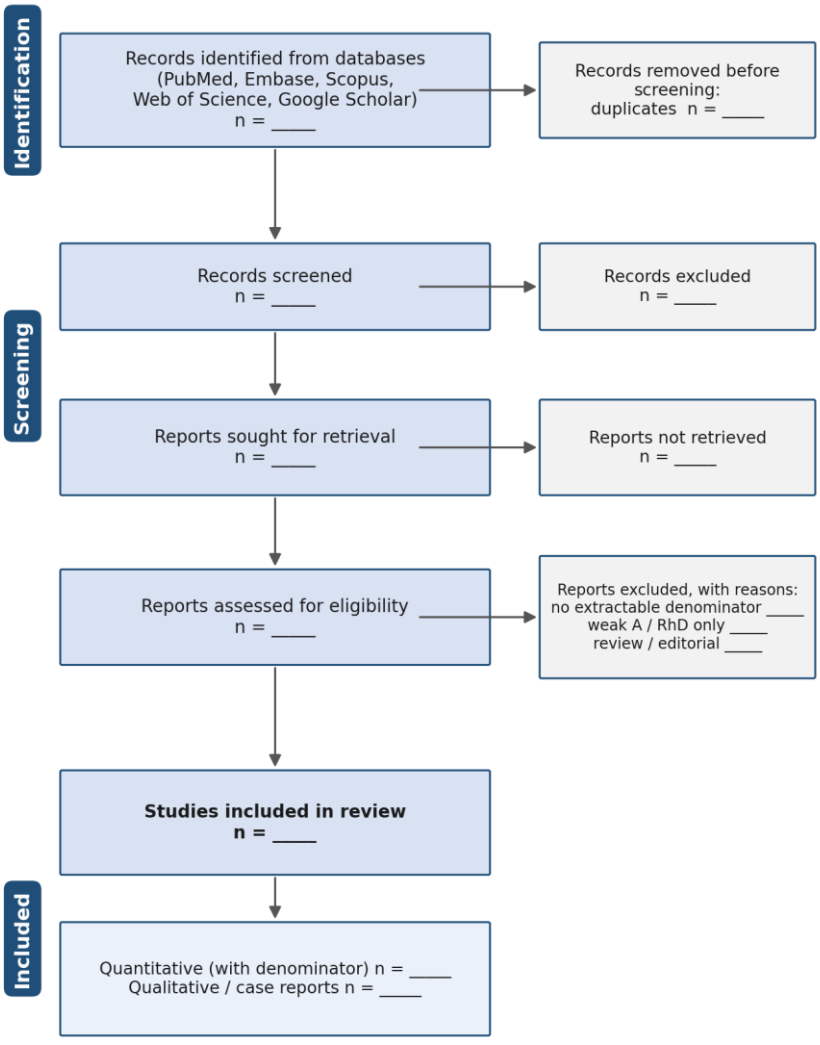

Figure 1. PRISMA 2020 flow diagram (count fields to be completed on the full registered search).

Figure 1. PRISMA 2020 flow diagram (count fields to be completed on the full search).

Table 1. Characteristics of located studies reporting weak/variant B (or ABO subgroup) frequency.

Study (country)	Design / period	Population & method	Denominator	Weak-B / subgroup finding
Eastern India cohort, 2024 [7]	Prospective; 2013–2021	Healthy donors; automated solid-phase (NEO Iris), adsorption–elution, saliva	84,534 donors (B = 29,190)	9 weak B (B3 4, Bm 3, Bx 1, Bel 1)

Wang et al., 2024 [8] (Shanghai)	Donor cohort; 2009–2017	Donors; automated microplate + DNA sequencing	2,945,643 samples	927 ABO subgroups (A+B); MDR 27.81%
Bhatia & Sathe, 1974 [9] (Bombay)	Donor/population series	Serological (incl. saliva, secretor)	Large Bombay series	Weak B variants ~1:24,000
Banerjee et al., 2021 [10] (S. India)	Case series	Forward/reverse + adsorption–elution + saliva	— (no denominator)	Weak B / para-Bombay B (qualitative)
Prasanth et al., 2025 [11] (Uttarakhand)	Case series (2)	Donors; adsorption–elution + saliva	— (no denominator)	2 ABel donors (qualitative)

MDR, missed-detection rate.

Risk of bias

A full JBI appraisal will follow once study selection is complete. The two large donor cohorts (Eastern India [7]; Shanghai [8]) relied on standardised automated measurement with serological and molecular confirmation, which supports valid case ascertainment; the dominant bias concern across this field is the opposite — under-ascertainment, as weak subgroups slip through routine testing. The Shanghai cohort put a figure on this, a 27.81% missed-detection rate, which pulls routine-method prevalence estimates downward [8].

Prevalence of weakly/variably expressed B antigen

Study-level estimates with exact 95% CIs appear in Table 2. In the Eastern Indian cohort, weak B occurred in 9 of 84,534 donors — **10.65 per 100,000** (95% CI 4.87–20.21), about 1 in 9,400 donors, or 0.031% of B-group donors [7]. By way of context, all ABO subgroups (A and B) in the Chinese cohort ran at 31.47 per 100,000 (95% CI 29.48–33.56) [8]. Since only one cohort offered a weak-B denominator in directly comparable form, the pre-set requirement for pooling — three or more cohorts — was not met, and no pooled estimate was produced; deriving one from a single study, or by mixing weak-B-specific and all-subgroup denominators, would not be sound. A defensible pooled value awaits the completed search.

Table 2. Study-level prevalence of weak B (and ABO subgroups) with exact 95% confidence intervals.

Phenotype (cohort)	**Cases / N**	**Per 100,000**	**95% CI (per 100,000)**
Weak B, overall (E. India) [7]	9 / 84,534	10.65	4.87 – 20.21
B3 (E. India) [7]	4 / 84,534	4.73	1.29 – 12.11
Bm (E. India) [7]	3 / 84,534	3.55	0.73 – 10.37
Bx (E. India) [7]	1 / 84,534	1.18	0.03 – 6.59
Bel (E. India) [7]	1 / 84,534	1.18	0.03 – 6.59
ABO subgroups, A+B (Shanghai) [8]	927 / 2,945,643	31.47	29.48 – 33.56

Exact (Clopper–Pearson) 95% CIs. The Shanghai row covers all ABO (A and B) subgroups, not weak B alone, and is shown for context only.

Subtype distribution and serological characterisation

Where subtypes were reported, B3 was the commonest weak B variant, then Bm, with Bx and Bel rarest (in the Eastern Indian cohort, B3 1 in 21,133; Bm 1 in 28,178; Bx and Bel each 1 in 84,534) [7]. Reactivity with anti-B and anti-AB ran from weak to 2+, sometimes with mixed-field appearances; a minority of donors were non-secretors, and adsorption–elution brought out B specificity at varying strengths. The donor case reports tell the same story from the bedside: a forward/reverse discordance — typically a B antigen missed on the forward group — is what prompts investigation, resolved by adsorption–elution, saliva testing and molecular work [10,11].

Molecular basis and genotype–phenotype correlation

The weak B phenotypes reflect quantitative or qualitative reductions in B-glycosyltransferase activity. Missense substitutions in the ABO gene — including changes lying outside the catalytic domain — can diminish enzyme efficiency and so lower B antigen density on the red cell, generating the weak or variable expression that defines B3, Bx, Bm and Bel [1,2]. In the large Chinese cohort, subgroups were resolved by direct DNA sequencing, underscoring molecular typing as the reference method when serology is equivocal and as the means of establishing genotype–phenotype correlation [8]. Systematic genotyping in future cohorts would let weak-B subtypes be mapped to defined alleles and would reduce the misclassification that follows from serology alone.

DISCUSSION

Several things emerge from the evidence assembled here. Weak B is uncommon — somewhere between 1 in 9,000 and 1 in 24,000 individuals across the cohorts identified [7,9] — and B3 is consistently the leading subtype. More consequential for daily practice is how often these phenotypes go unrecognised: the Shanghai cohort placed the missed-detection rate at 27.81%, which means conventional prevalence figures almost certainly understate the true burden [8]. The literature itself is fragmented, dominated by single-centre series whose denominators and detection methods differ enough to exaggerate apparent variation and to make uncritical pooling inappropriate.

These points bear directly on the safety of ABO typing. A weak or variant B antigen reacts faintly or not at all with anti-B; on a low-sensitivity forward method such as the slide technique, which is known to miss weakly expressed reactions [3], the result can be a false-negative anti-B and a discrepancy that goes unnoticed. The protection is structural rather than incidental — reverse grouping, which exposes the missing anti-B, backed by confirmation through sensitive methods (tube or column agglutination, adsorption–elution, saliva and molecular typing) before any B-containing group is signed out. The discrepancy literature reinforces this, since the weak/missing-antigen (Type II) discrepancy is exactly what these phenotypes produce [4].

Clinically, calling a weak B an O or an A can lead to the issue of unsuitable components and, for plasma-containing products, to incompatibility; getting the phenotype right safeguards both donor classification and recipient safety. The underlying biology — missense changes in the B glycosyltransferase, some lying outside the catalytic domain — accounts for the reduced antigen output that defines these variants [1,2] and makes molecular typing the reference standard when serology is equivocal.

Clinical Implications for Transfusion Services

Because a weakly expressed B antigen typically presents as a forward/reverse discordance — a B antigen under-detected on the forward group set against a serum that lacks the expected anti-B — transfusion services benefit from a standard, escalating resolution pathway rather than ad hoc retesting. Figure 2 sets out such an algorithm. After clerical and technical error is excluded and the full forward and reverse panel repeated by tube or column agglutination, weak reactions are enhanced (increased serum-to-cell ratio, room-temperature and 4 °C incubation with appropriate controls, and extended incubation). The antigen is then demonstrated by adsorption–elution and by saliva testing for secreted B and H substances, and the subgroup is confirmed and typed by ABO genotyping. Mimics — recent transfusion or transplantation with chimerism, acquired B, and disease-related antigen depression — are excluded, and historical records are reviewed. Until the discrepancy is resolved, conservative component selection (group O red cells and AB plasma, as appropriate to the product) protects the patient [12,4].

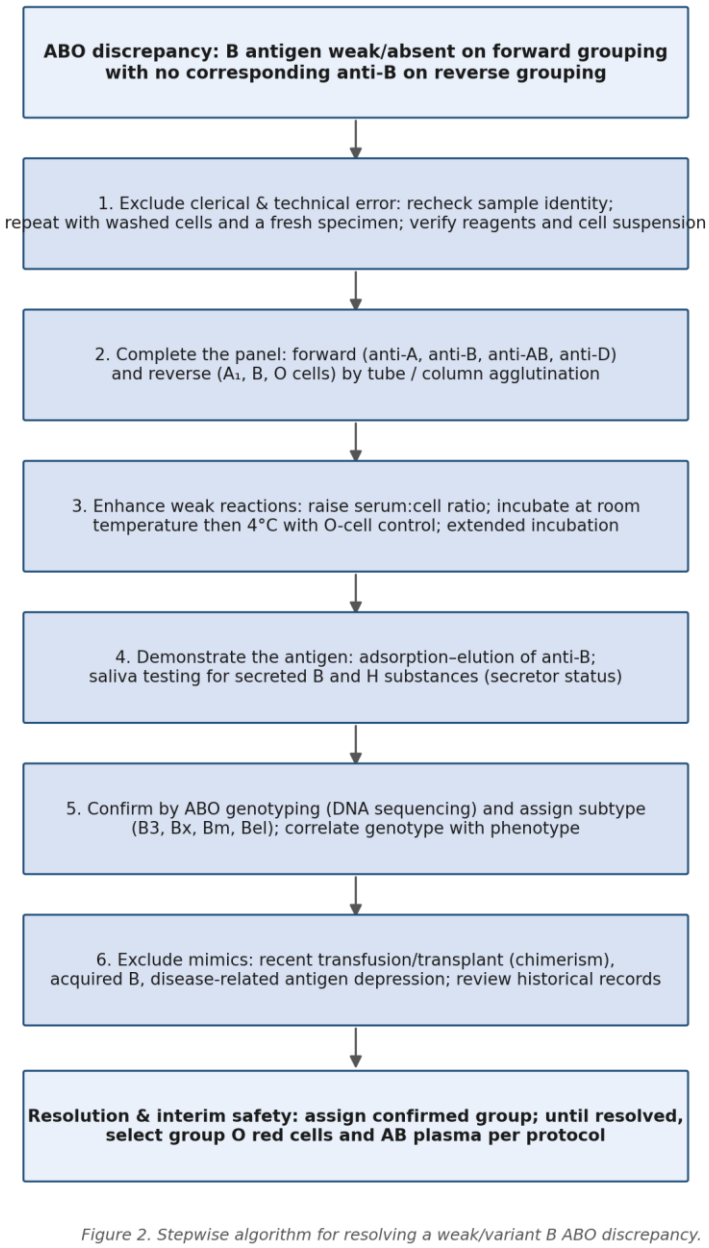

Figure 2. Stepwise algorithm for resolving a weak/variant B ABO discrepancy.

Figure 2. Stepwise algorithm for resolving a weak/variant B ABO discrepancy.

limitations

The quantitative findings reported here come from a targeted preliminary search and should be read as provisional until the full multi-database search and PRISMA census are complete; the review was also not prospectively registered, which carries a risk of selection and reporting bias. The evidence base is geographically narrow, drawn almost entirely from Indian and Chinese cohorts, which limits generalisability to populations in which ABO allele frequencies differ. Cohorts with an extractable weak-B denominator proved few, which is why no valid pooled estimate could be produced, and heterogeneity in any eventual pool is likely to be extreme (I^2 approaching 100% is typical of prevalence meta-analyses). Variation in detection method — manual slide testing, automated solid-phase platforms and molecular assays — both complicates comparison and may inflate apparent variability, and publication and language effects may distort the available figures further.

CONCLUSION

Weakly or variably expressed B antigen is rare but clinically consequential, and it is routinely under-detected by ordinary forward grouping. The available cohorts put its donor prevalence at roughly 1 in 9,000 to 1 in 24,000, with B3 to the fore, while missed-detection data suggest the real figure is higher. A definitive pooled prevalence

must wait on the full, systematic multi-database search; the practical message, however, is already firm — forward and reverse grouping should agree, confirmed by sensitive and, where needed, molecular methods, before any B-containing ABO group is reported.

Declarations

Ethical approval: Not required; this is a systematic review of previously published, aggregated data and involved no new human or animal participants.

Conflict of interest: The author declares no conflict of interest.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability: All data analysed in this review derive from the cited published studies; the extraction sheets are available from the corresponding author on reasonable request.

Registration: This review was not registered in a prospective registry.

REFERENCES

1. Storry, J. R., & Olsson, M. L. (2009). The ABO blood group system revisited: A review and update. Immunohematology, 25(2), 48–59. https://doi.org/10.21307/immunohematology-2019-231
2. Seltsam, A., & Blasczyk, R. (2005). Missense mutations outside the catalytic domain of the ABO glycosyltransferase can cause weak blood group A and B phenotypes. Transfusion, 45(10), 1663–1669. https://doi.org/10.1111/j.1537-2995.2005.00558.x
3. Li, H.-Y., & Guo, K. (2022). Blood group testing. Frontiers in Medicine, 9, 827619. https://doi.org/10.3389/fmed.2022.827619
4. Desai, P., Navkudkar, A., & Rajadhyaksha, S. (2024). ABO blood group discrepancies in blood donor and patient samples at a tertiary care oncology centre: Analysis and serological resolution. Hematology, Transfusion and Cell Therapy, 46(4), 402–407. https://doi.org/10.1016/j.htct.2023.07.011
5. Thakral, B., Saluja, K., Bajpai, M., Sharma, R. R., & Marwaha, N. (2005). Importance of weak ABO subgroups. Laboratory Medicine, 36(1), 32–34.
6. Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., et al. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ, 372, n71. https://doi.org/10.1136/bmj.n71
7. Prevalence of “weak B” phenotypes and their evaluation and differentiation in healthy blood donor population in Eastern India. (2024). Asian Journal of Transfusion Science, 18(2), 225–229. https://doi.org/10.4103/ajts.ajts_36_23
8. Wang, Z., Jin, S., Zheng, J., Qian, C., Cai, X., & Xiang, D. (2024). Prevalence and distribution of serological characteristics of weak ABO subgroups in the Chinese population. Hematology, Transfusion and Cell Therapy, 46, S115–S121. https://doi.org/10.1016/j.htct.2024.04.127
9. Bhatia, H. M., & Sathe, M. S. (1974). Incidence of “Bombay” (Oh) phenotype and weaker variants of A and B antigen in Bombay (India). Vox Sanguinis, 27, 524–532.
10. Banerjee, S., Alwar, V. A., & Subramanian, S. (2021). The importance of testing for secretor status of ABH antigens: A case series. Iraqi Journal of Hematology, 10(2), 176–179. https://doi.org/10.4103/ijh.ijh_25_21
11. Prasanth, V., Banerjee, P., Kaur, D., Kumari, D., Khiamniungan, C. B., Bhatia, J., Jain, A., & Negi, G. (2025). A or AB? Resolving the dilemma of weaker subgroup through serological evaluation: Reporting two cases from Uttarakhand. Asian Journal of Transfusion Science, 19(1), 154–157. https://doi.org/10.4103/ajts.ajts_154_23
12. Meny, G. M. (2017). Recognizing and resolving ABO discrepancies. Immunohematology, 33(2), 76–81.